



US 20080082306A1

(19) **United States**(12) **Patent Application Publication****Jung et al.**(10) **Pub. No.: US 2008/0082306 A1**(43) **Pub. Date: Apr. 3, 2008**(54) **COMPUTATIONAL SYSTEMS FOR  
BIOMEDICAL DATA****Related U.S. Application Data**(63) Continuation-in-part of application No. 11/541,478,  
filed on Sep. 29, 2006.**Publication Classification**(51) **Int. Cl.**  
**G06G 7/48** (2006.01)(52) **U.S. Cl.** ..... 703/11(57) **ABSTRACT**

Methods, apparatuses, computer program products, devices and systems are described that carry out accepting an input providing innate determinant data from at least one sample, accessing a dataset to identify, based on the innate determinant data, at least one innate allergy determinant in the at least one sample; accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information; and presenting a signal related to ingestion-dependent allergy predisposition information in response to accessing the allergy test dataset to identify, based on the at least one innate allergy determinant, the allergy predisposition information.

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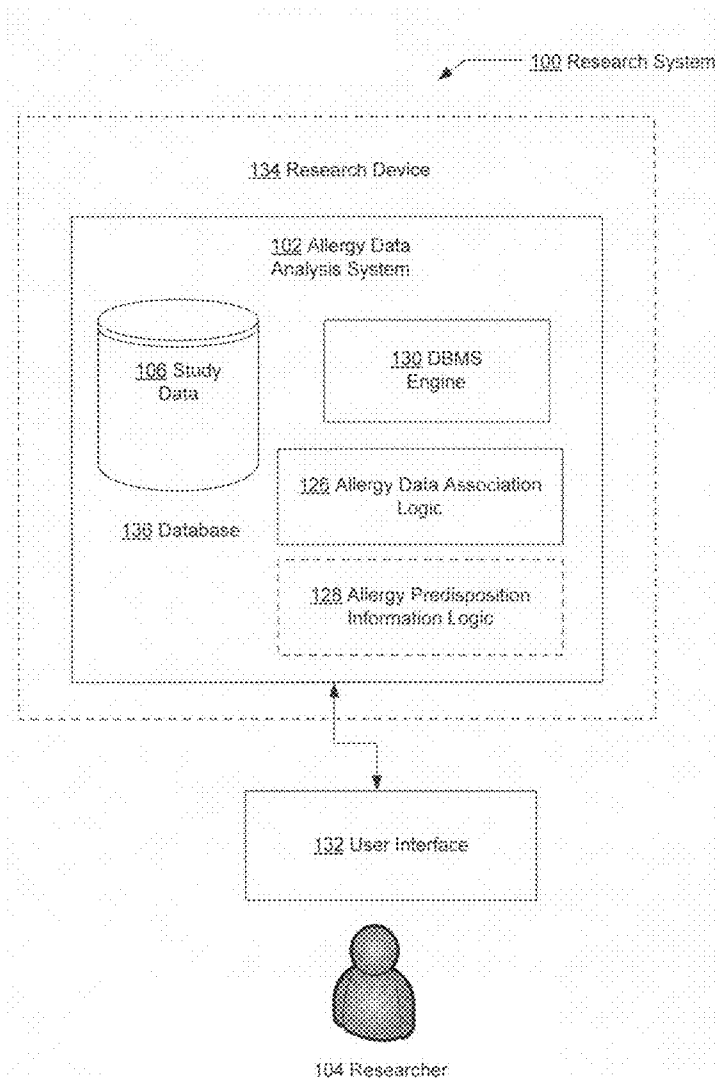
(73) Assignee: **Searete LLC**(21) Appl. No.: **11/728,026**(22) Filed: **Mar. 22, 2007**

FIG. 1

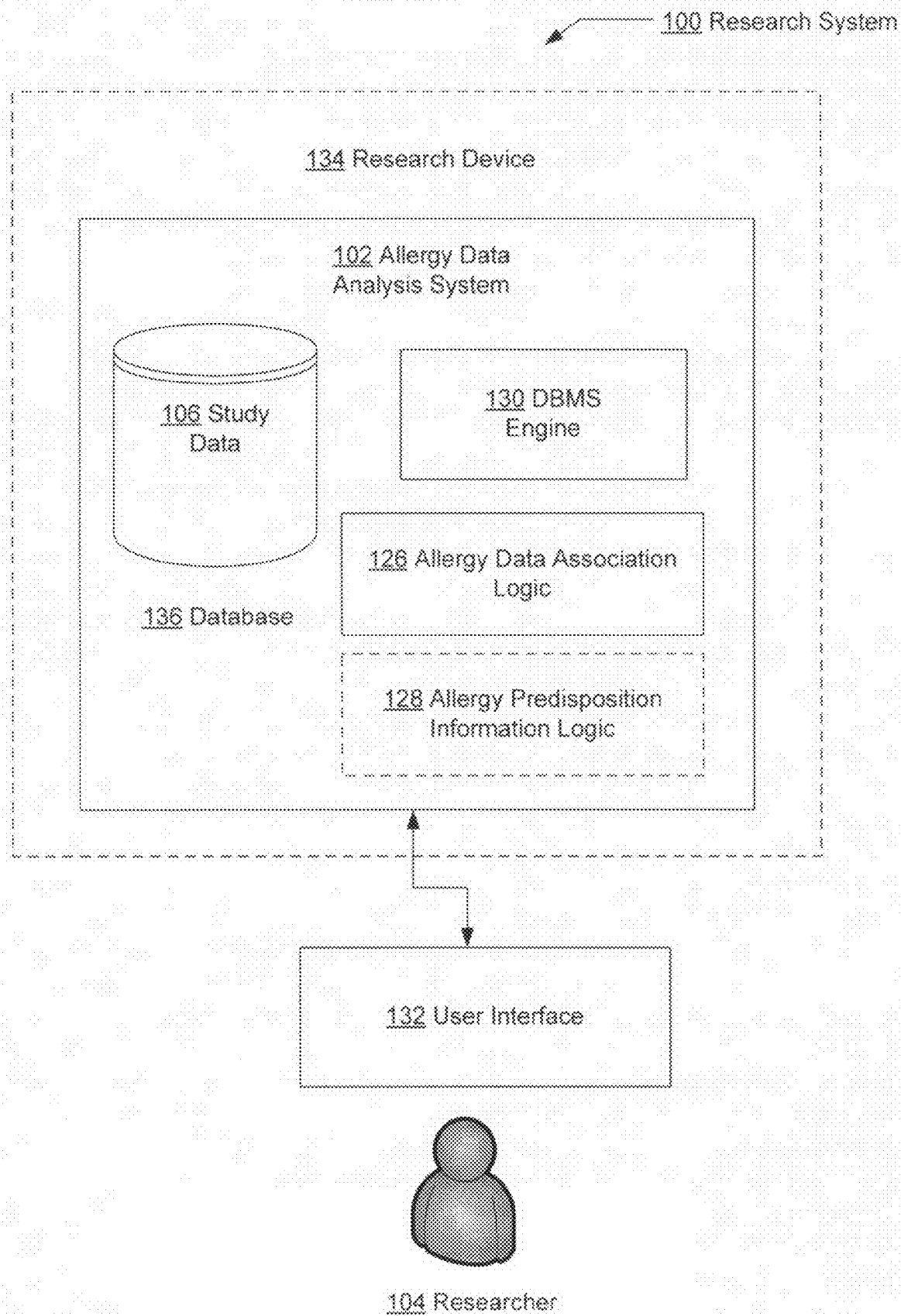


FIG. 2

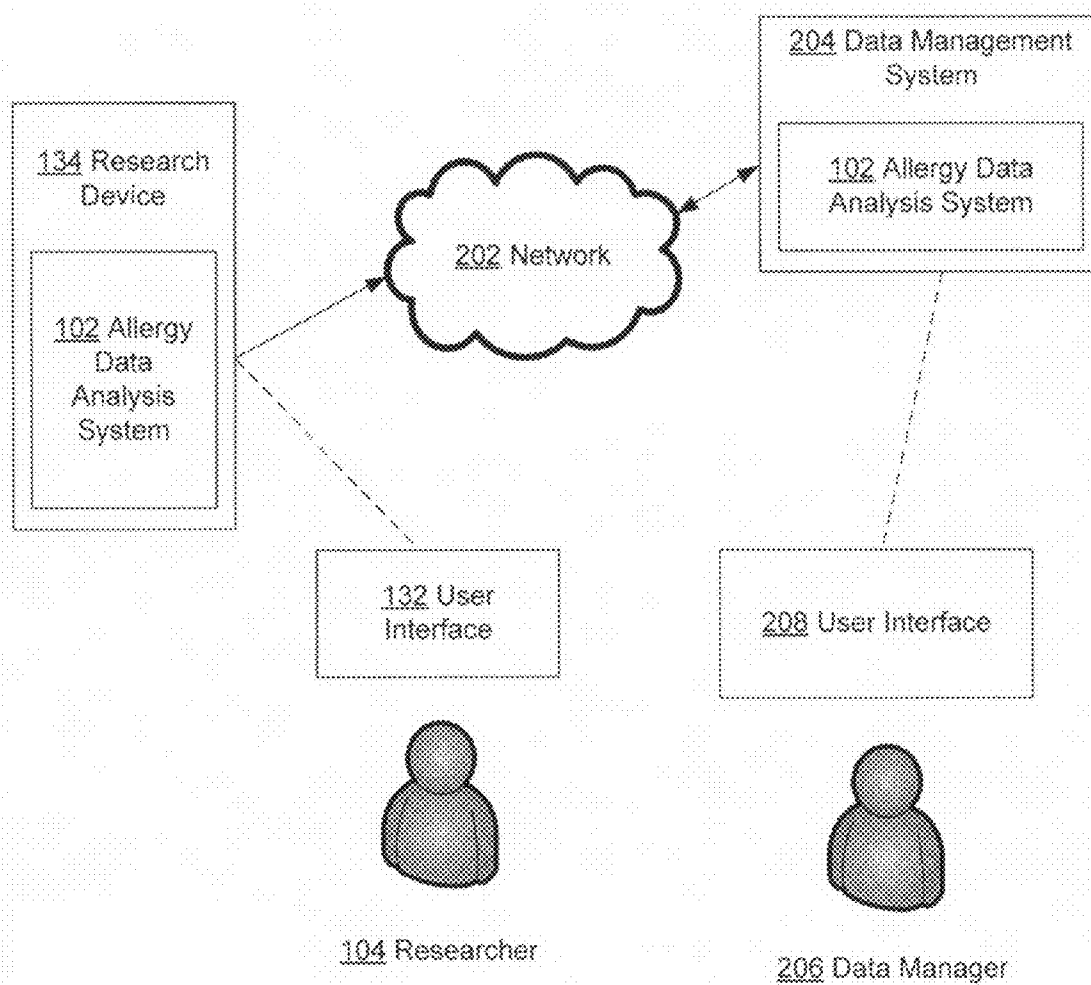


FIG. 3

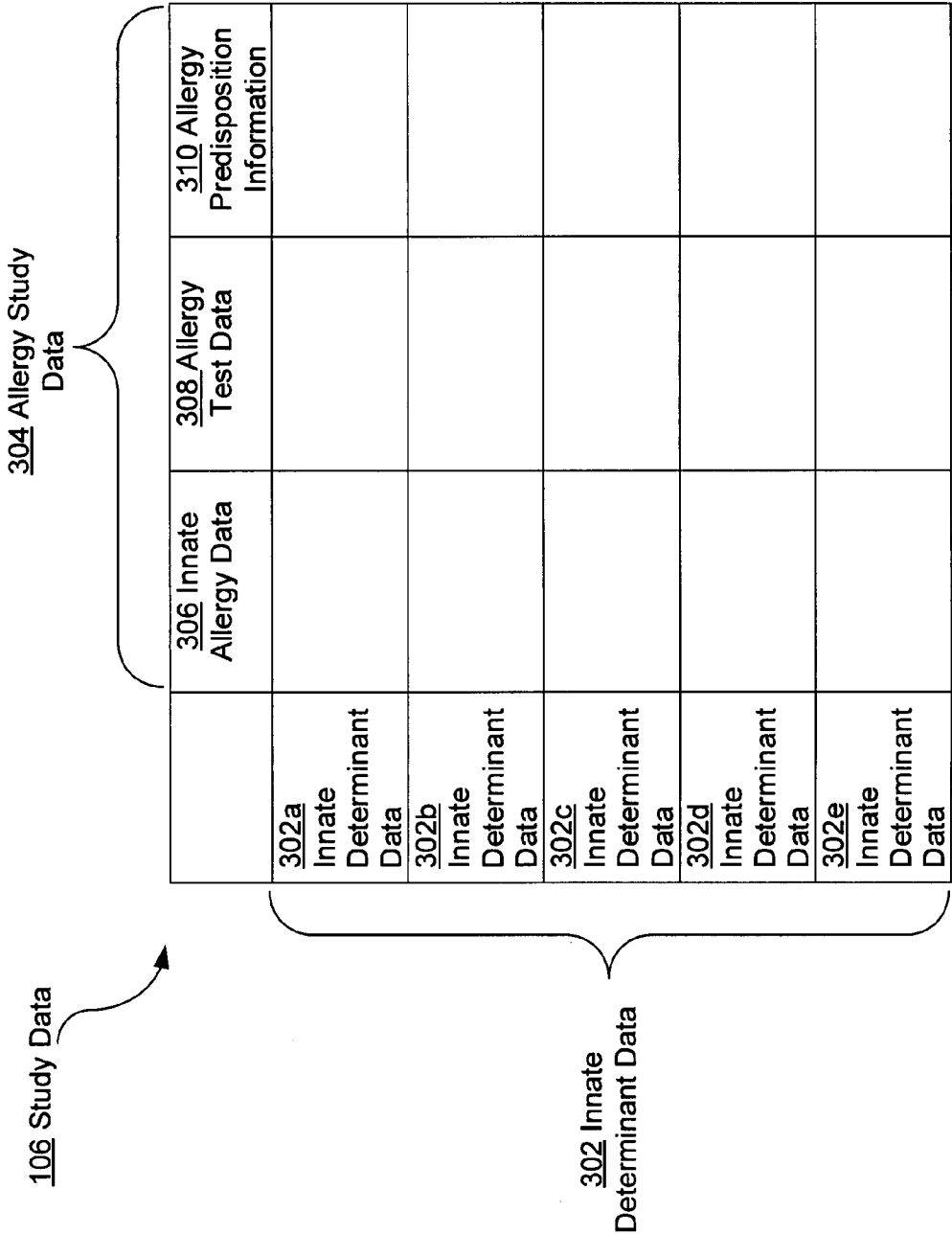


FIG. 4

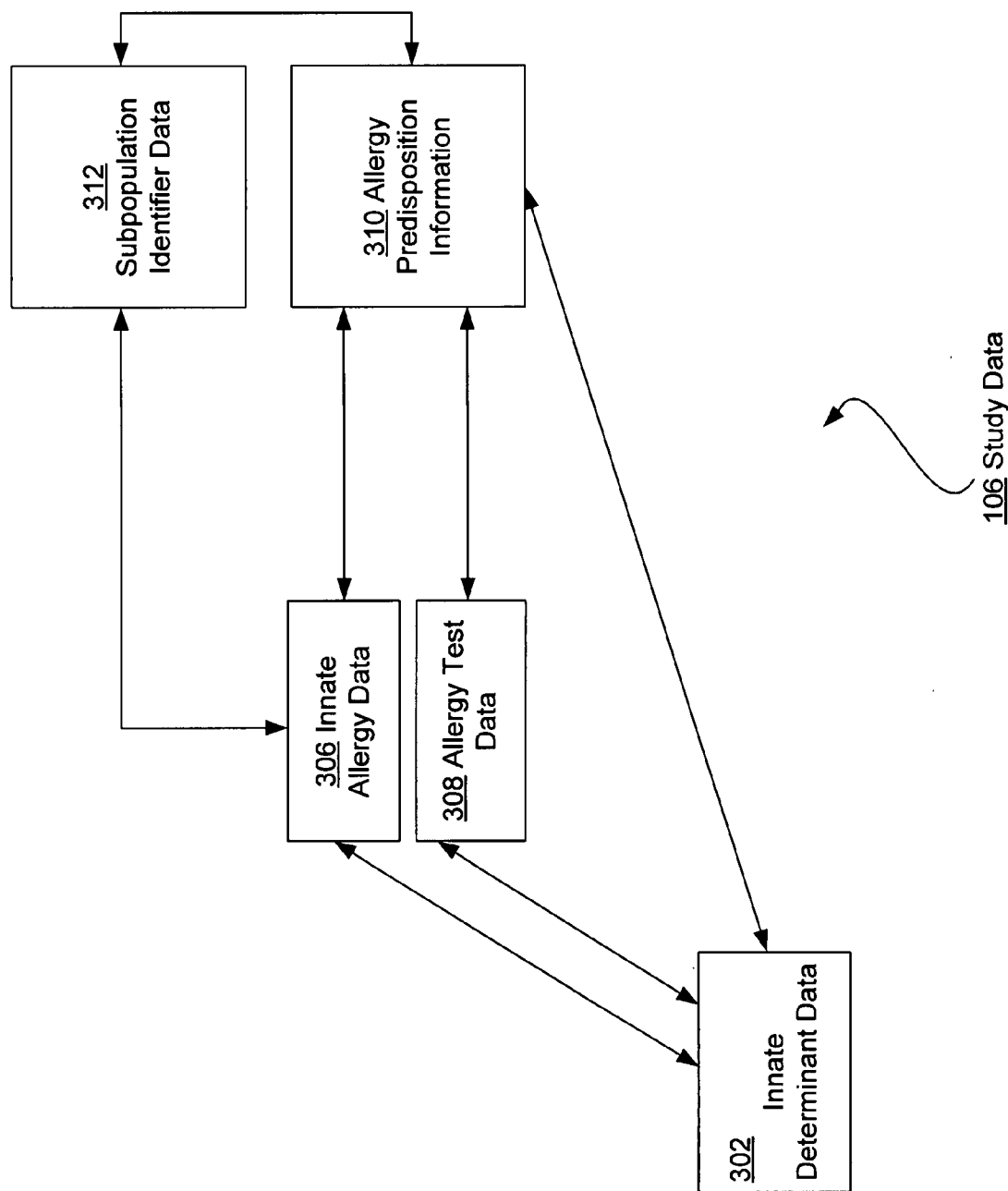


FIG. 5

	<u>306</u> Innate Allergy Data	<u>308</u> Allergy Test Data	<u>310</u> Allergy Predisposition Information
502 CARD4/-21596 "TT" polymorphism	CARD4/-21596 "TT" polymorphism associated with pollen allergy	Specific IgE $\geq$ 3.5 IU/ml indicative of pollen allergy	Frequency of farmers' children having specific IgE to pollen $\geq$ 3.5 is 5.8%
504 CARD4/-21596 "CC/CT" polymorphism	CARD4/-21596 "CC/CT" polymorphism associated with house dust mite allergy	Specific IgE $\geq$ 3.5 IU/ml indicative of house dust mite allergy	Frequency of farmers' children having specific IgE to house dust mite $\geq$ 3.5 is 14.3%;
506 CARD4/-21596 "TT" polymorphism	CARD4/-21596 "TT" polymorphism associated with cat dander allergy	Specific IgE $\geq$ 3.5 IU/ml indicative of cat dander allergy	Frequency of farmers' children having specific IgE to cat dander $\geq$ 3.5 is 0.0%
508 CARD4/-21596 "TT" polymorphism	CARD4/-21596 "TT" polymorphism associated with hay fever allergy	Doctor's diagnosis of hay fever	Frequency of farmers' children having specific IgE to hay fever $\geq$ 3.5 is 13.0%

FIG. 6

	306 Innate Allergy Data	308 Allergy Test Data	310 Allergy Predisposition Information
HLA DR9 genotype	HLA DR9 genotype associated with penicillin allergy	Patients positive for penicillin IgE antibodies	11.04% of HLA DR9 patients with allergic reaction; 6.25% of HLA DR9 patients with positive penicillin IgE antibodies; 12.16% of HLA DR9 patients with immediate reaction; and 13.51% of HLA DR9 patients with urticaria (compared to 4.02% of control subjects with an HLA DR9 allele)
HLA DR14.1 genotype	HLA DR14.1 genotype associated with penicillin allergy	Patients positive for penicillin IgE antibodies	0% of HLA DR14.1, penicillin IgE-positive patients with an immediate reaction; and 0% of HLA DR14.1, penicillin IgE-positive patients with urticaria (compared to 9.77% of control subjects with an HLA DR14.1 allele)

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FIG. 7

	<u>306</u> Innate Allergy Data	<u>308</u> Allergy Test Data	<u>310</u> Allergy Predisposition Information
ALOX 5 genotype (non5/non5)	ALOX 5 genotype (non5/non5) associated with asthma	Eosinophil count = 390	Moderate-severe symptoms in individuals with the ALOX5 non5/non5 genotype; and an eosinophil count of 280 vs. 390 in moderate-severe individuals
ALOX 5 genotype (non5/non5)	ALOX 5 genotype (non5/non5) association with asthma	Total IgE = 229	5.3% of individuals with the ALOX5 non5/non5 genotype reported moderate-severe symptoms vs. 1.4% with mild symptoms; moderate-severe individuals had total IgE of 229 vs. 179 in the mild group
ALOX 5 genotype (non5/non5)	ALOX 5 genotype (non5/non5) association with asthma	Eosinophil count = 390	Odds ratio of having moderate-severe asthma = 3.647 in ALOX5 non5/non5 individuals vs. other ALOX5 alleles

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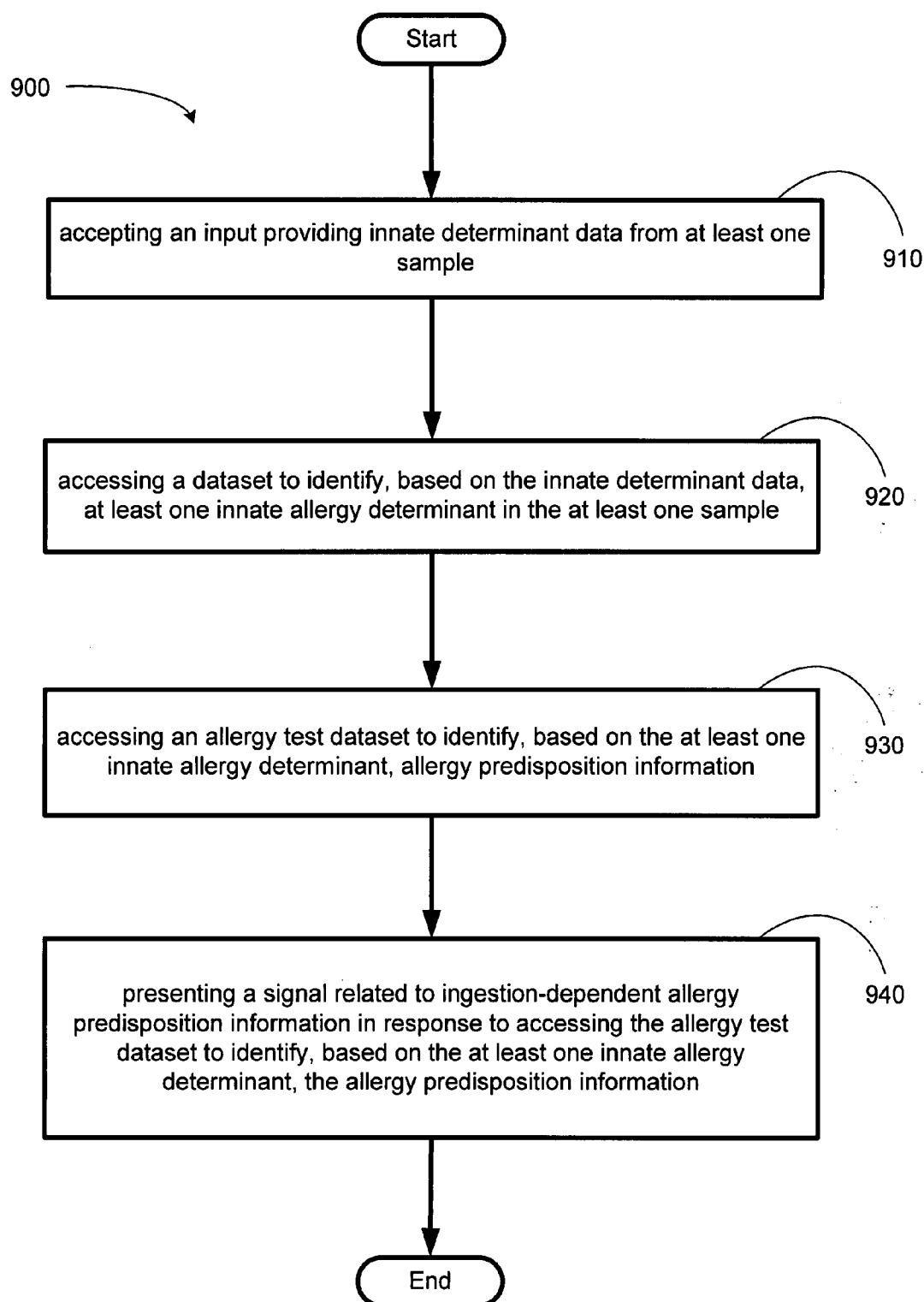
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FIG. 8

	306 Innate Allergy Data	308 Allergy Test Data	810 Ingestion-dependent Allergy Predisposition Information
802	DNA sequence	Specific IgE to peanut allergen measurement	Peanut allergy symptoms associated with the DNA sequence peanut allergy determinant and the specific IgE to peanut allergen
804	Epigenetic determinant	Total IgE measurement	Degree of peanut allergy symptoms associated with the epigenetic peanut allergy determinant and the total IgE measurement
806	Gene expression determinant	Eosinophil count	Incidence of peanut allergy symptoms associated with the gene expression peanut allergy determinant and the eosinophil count

FIG. 9



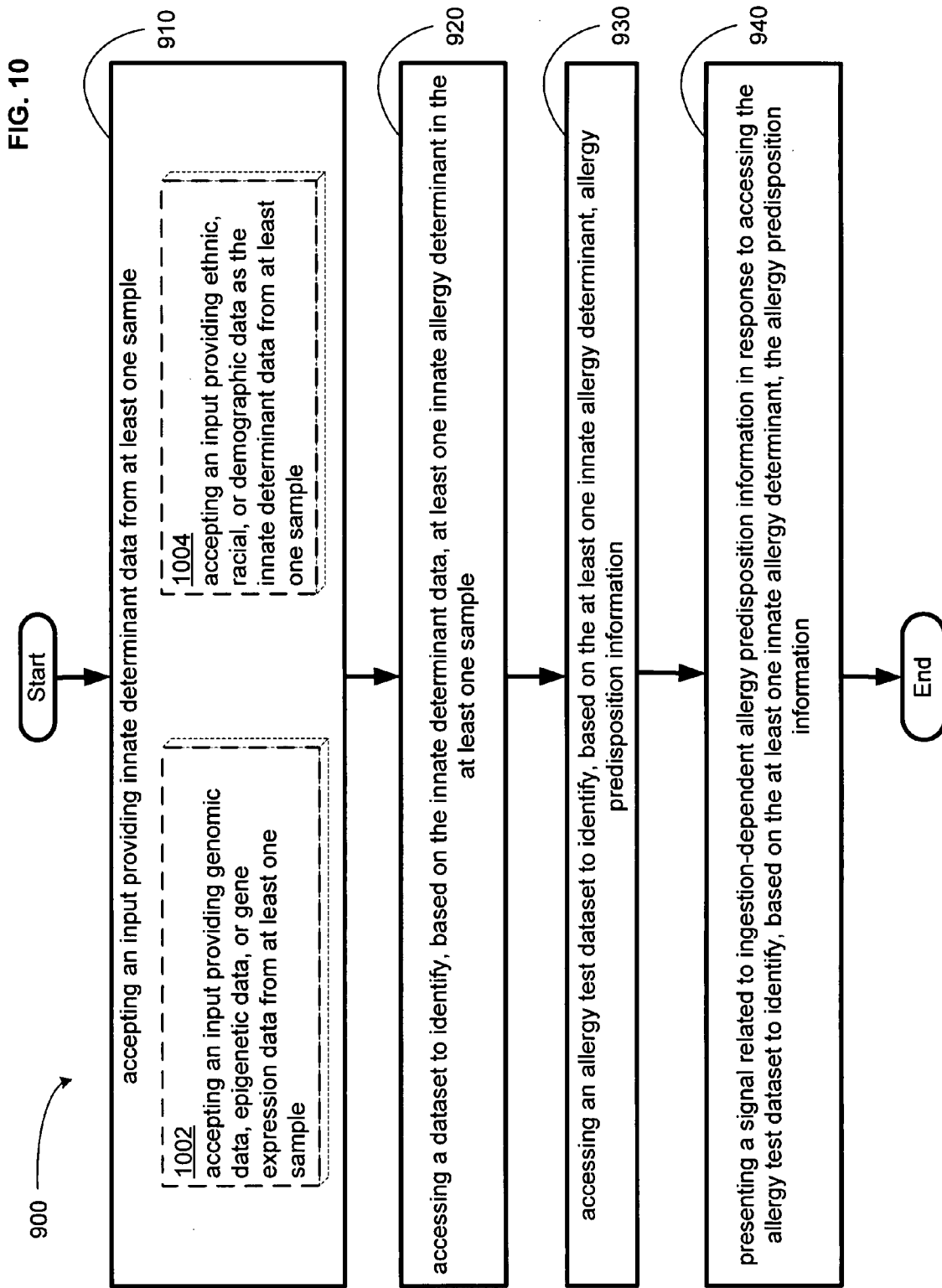
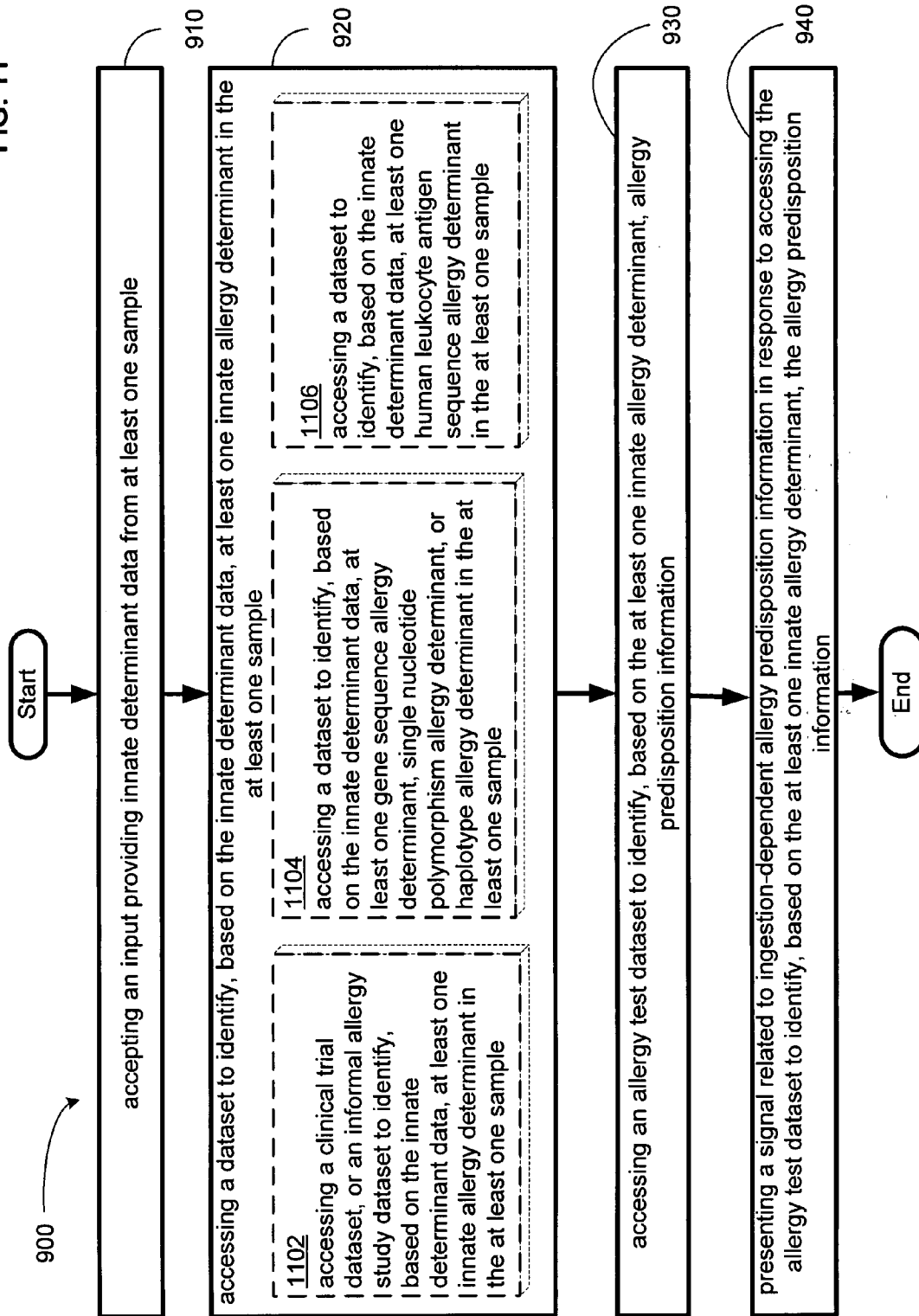


FIG. 11



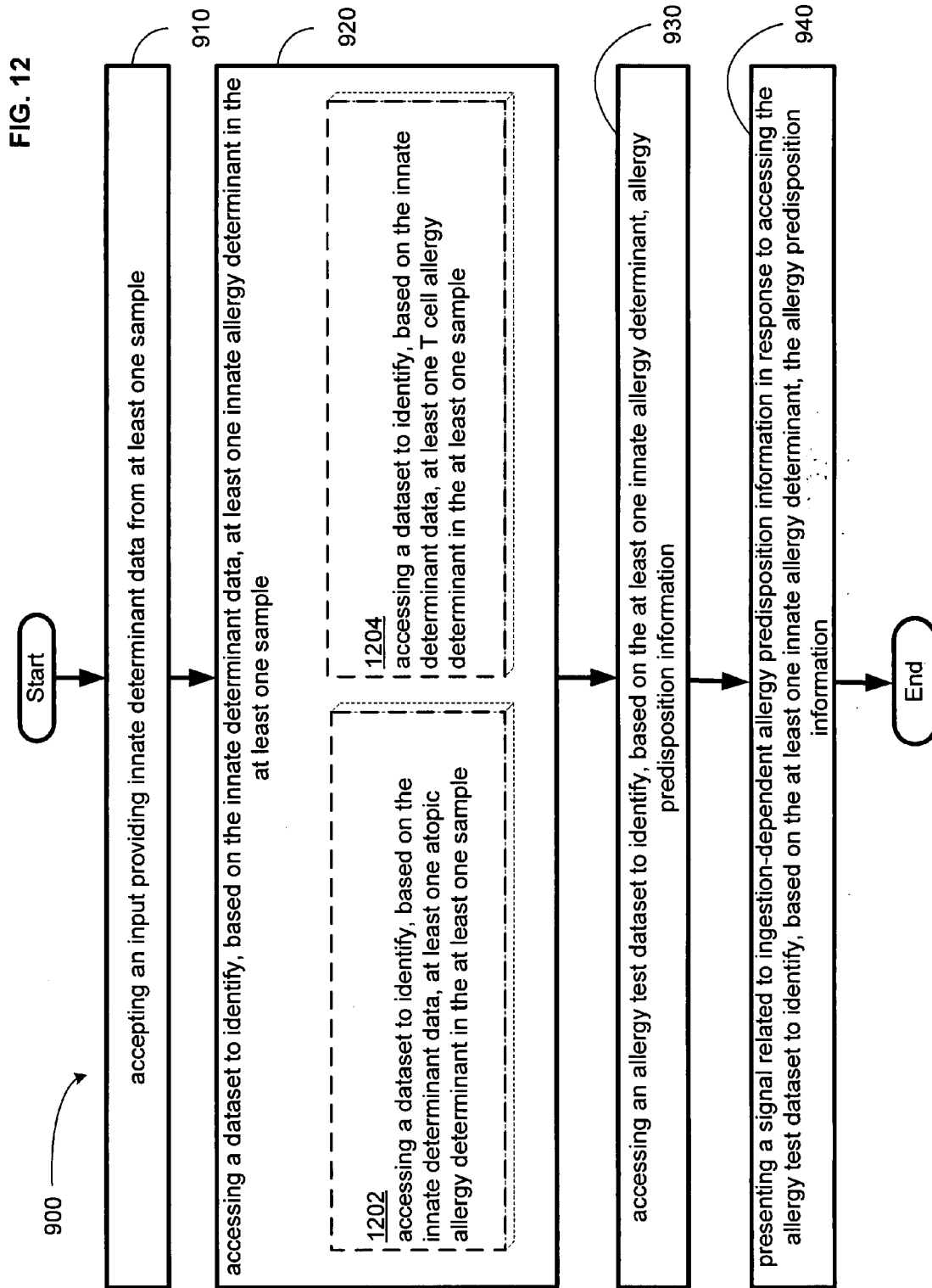


FIG. 13

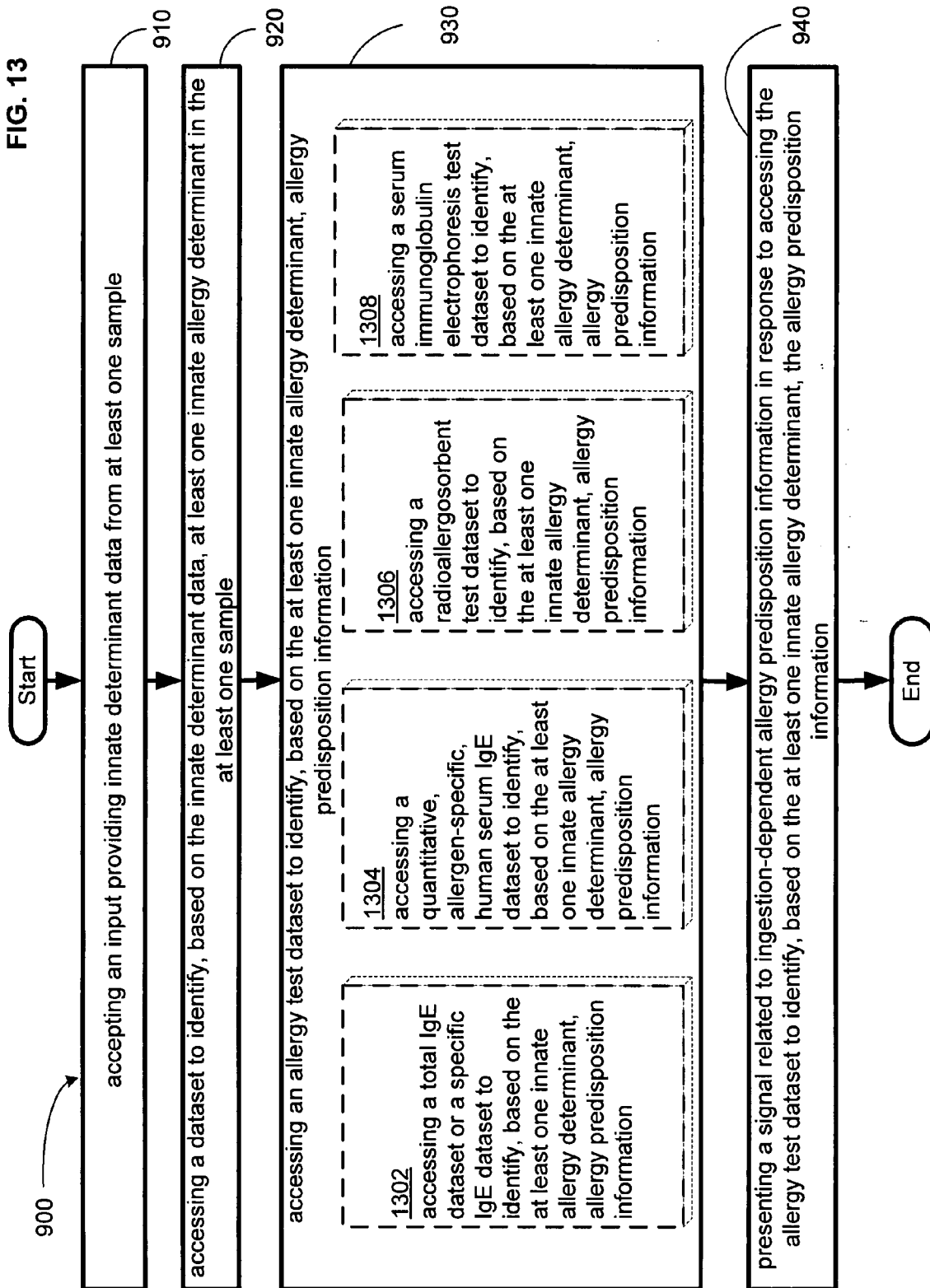
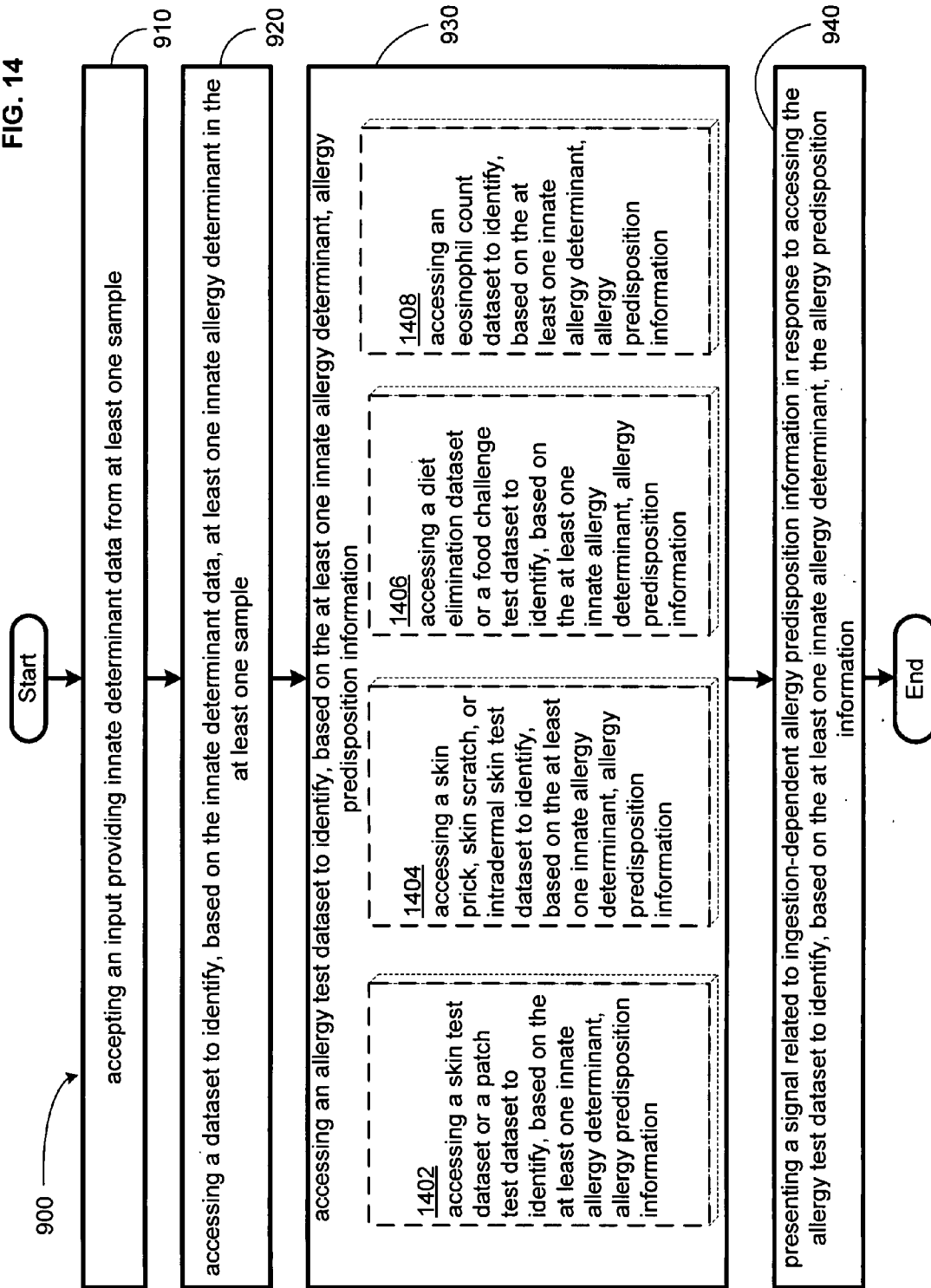
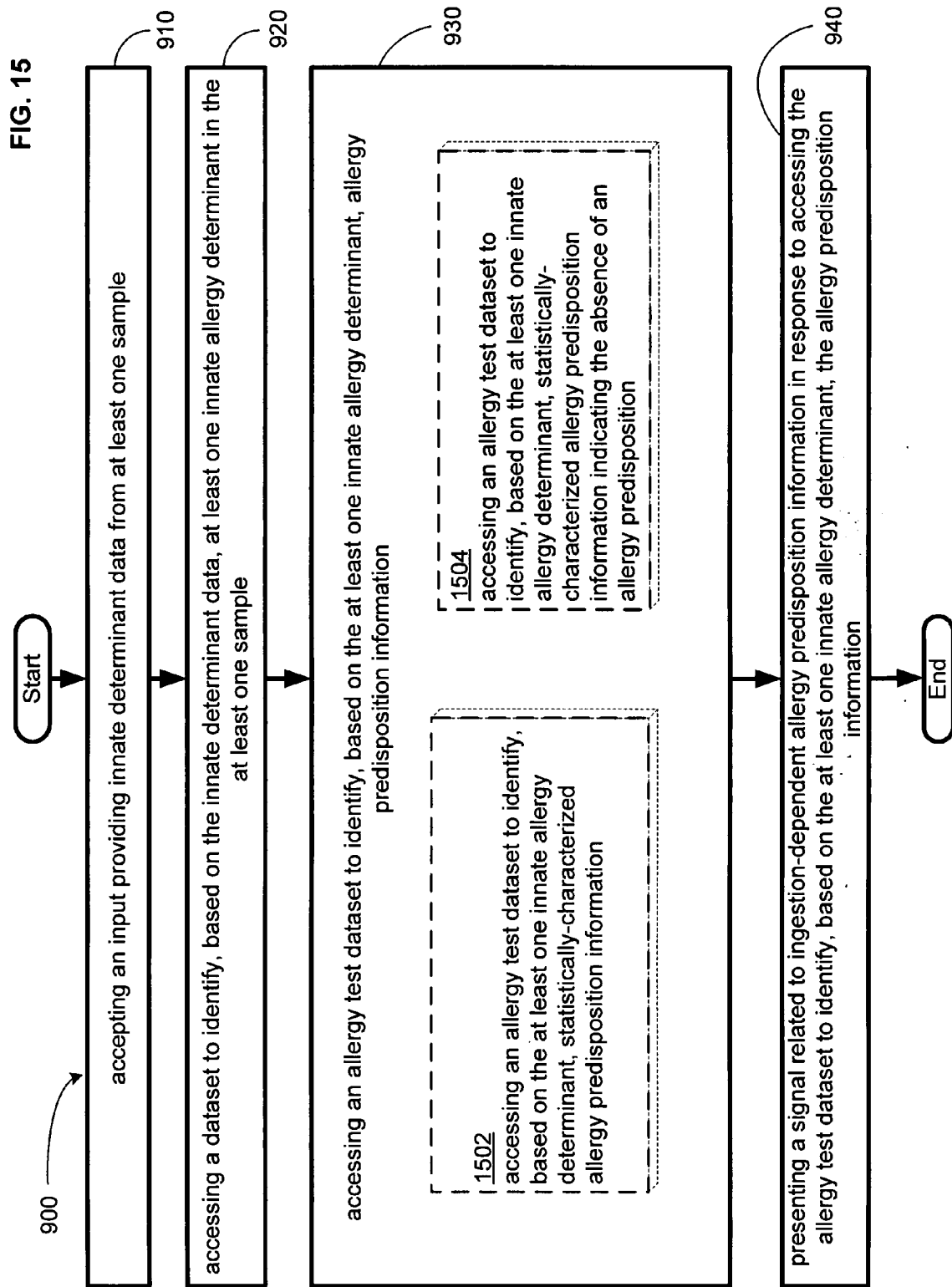


FIG. 14







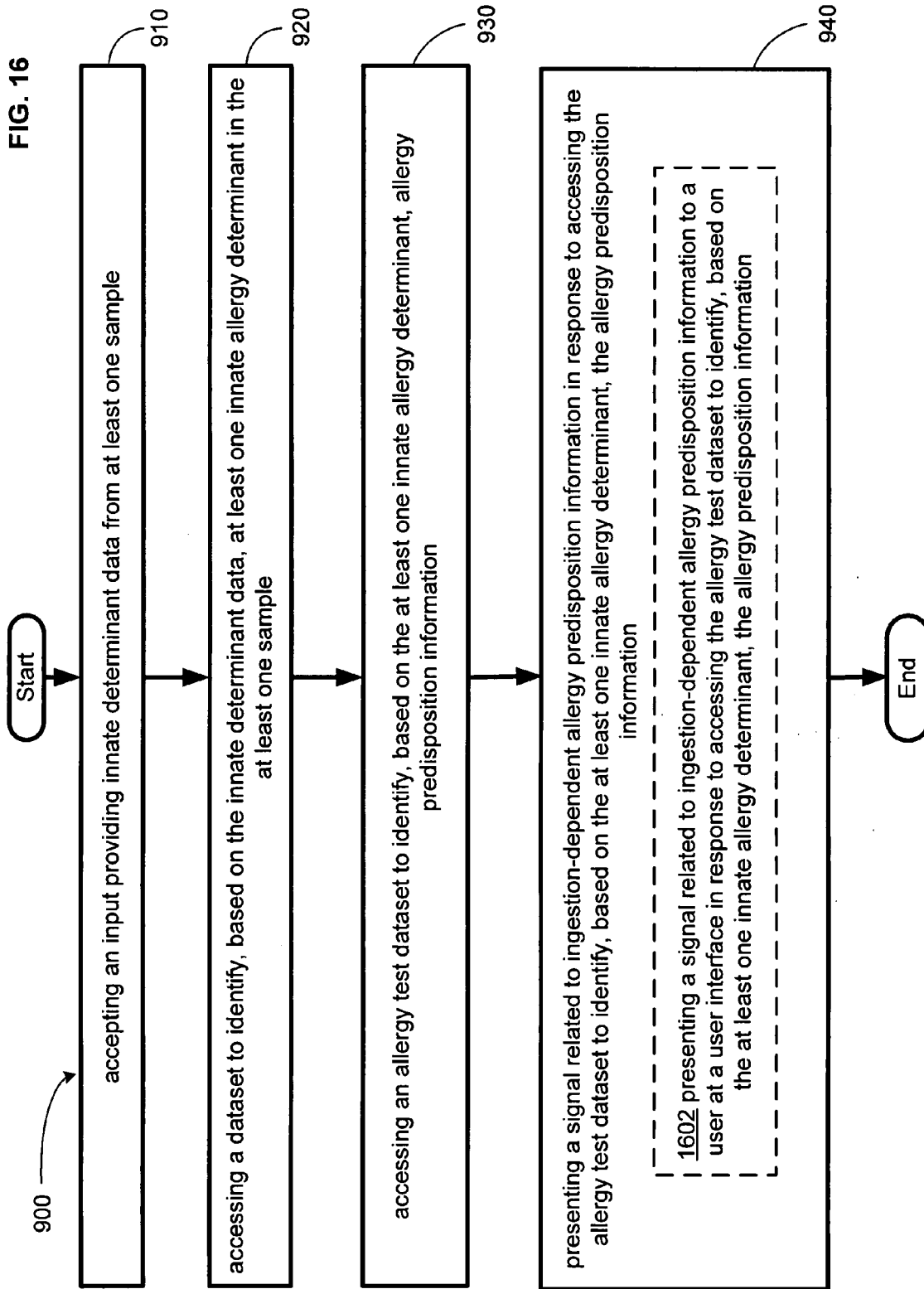
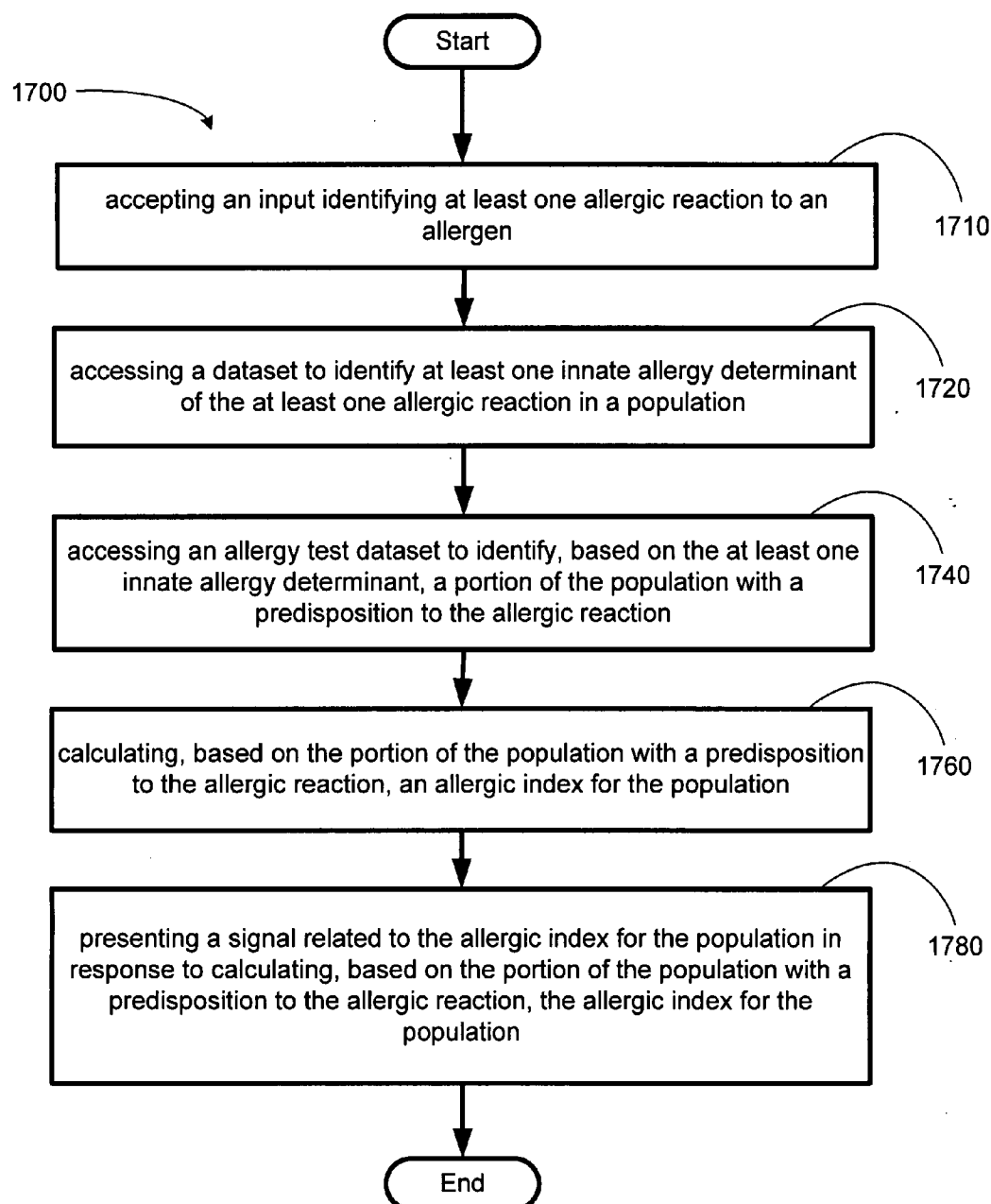


FIG. 17



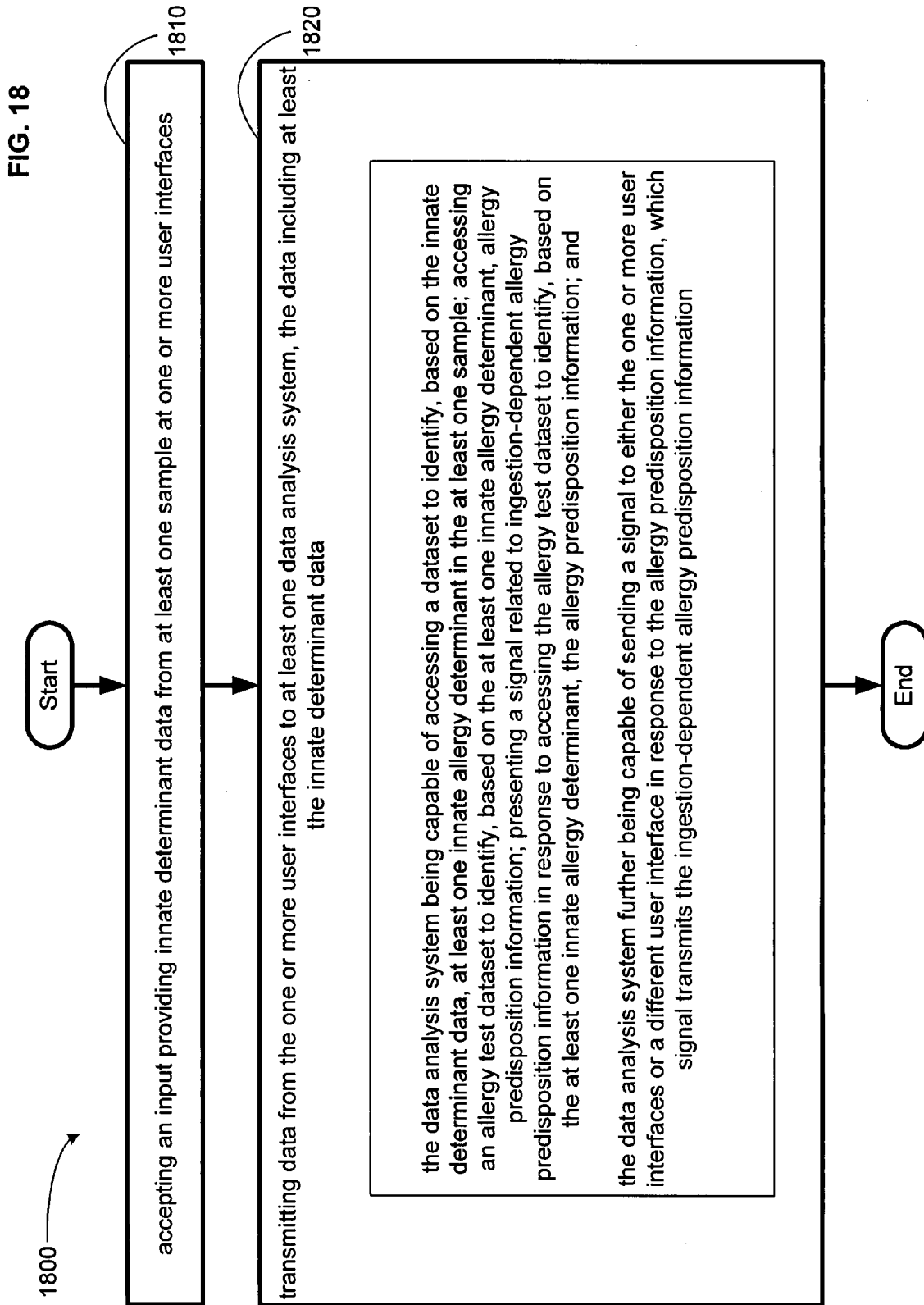


FIG. 19

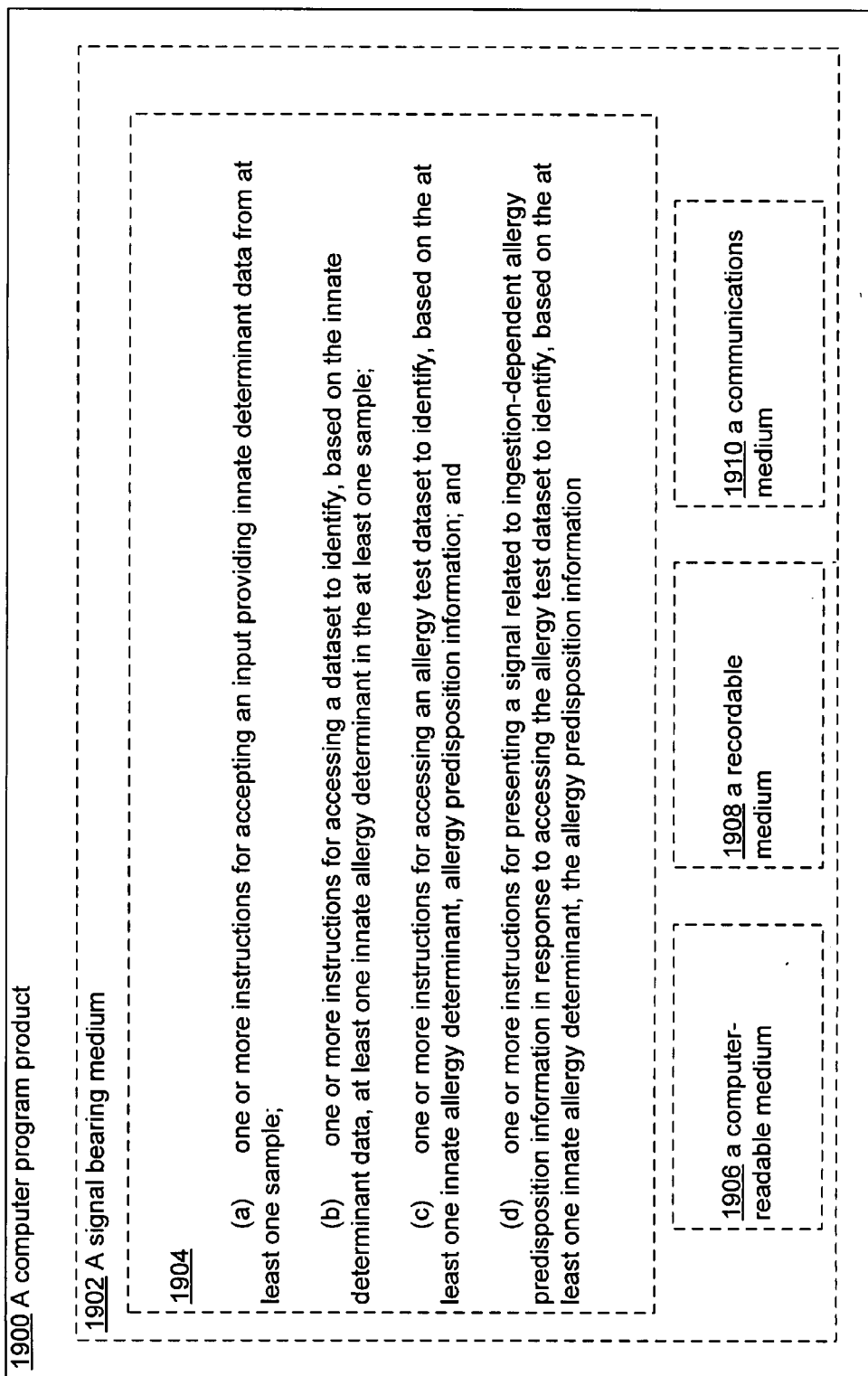
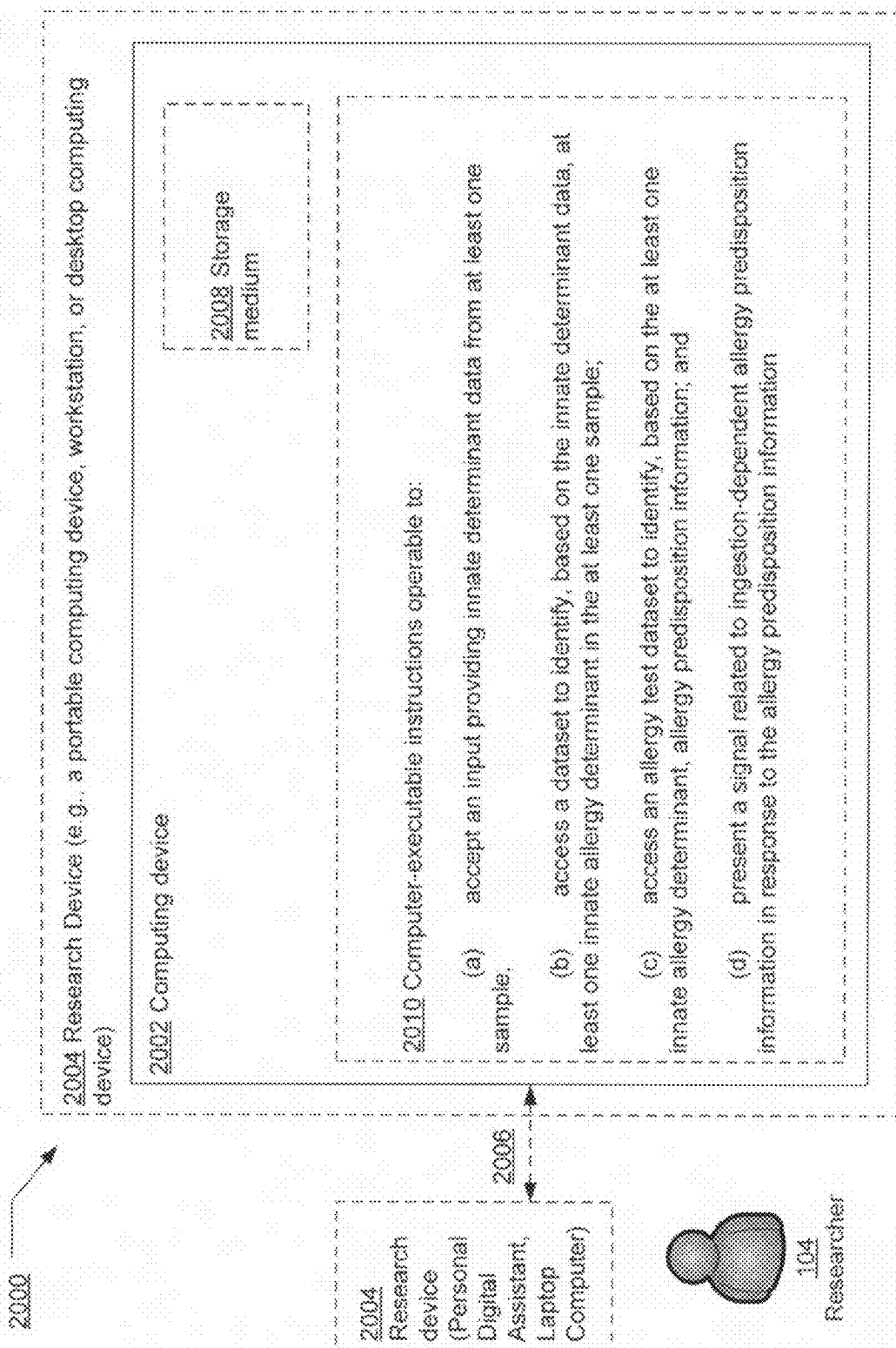


FIG. 20



## COMPUTATIONAL SYSTEMS FOR BIOMEDICAL DATA

### CROSS-REFERENCE TO RELATED APPLICATIONS

**[0001]** The present application is related to and claims the benefit of the earliest available effective filing date(s) from the following listed application(s) (the "Related Applications") (e.g., claims earliest available priority dates for other than provisional patent applications or claims benefits under 35 USC § 119(e) for provisional patent applications, for any and all parent, grandparent, great-grandparent, etc. applications of the Related Application(s)).

### RELATED APPLICATIONS

**[0002]** For purposes of the USPTO extra-statutory requirements, the present application constitutes a continuation-in-part of U.S. patent application Ser. No. 11/541,478, entitled COMPUTATIONAL SYSTEMS FOR BIOMEDICAL DATA, naming Edward K. Y. Jung; Royce A. Levien; Robert W. Lord and Lowell L. Wood, Jr. as inventors, filed 29 Sep. 2006 which is currently co-pending, or is an application of which a currently co-pending application is entitled to the benefit of the filing date.

**[0003]** For purposes of the USPTO extra-statutory requirements, the present application constitutes a continuation-in-part of U.S. patent application Ser. No. 11/647,531, entitled COMPUTATIONAL SYSTEMS FOR BIOMEDICAL DATA, naming Edward K. Y. Jung; Royce A. Levien; Robert W. Lord and Lowell L. Wood, Jr. as inventors, filed 27 Dec. 2006 which is currently co-pending, or is an application of which a currently co-pending application is entitled to the benefit of the filing date.

**[0004]** For purposes of the USPTO extra-statutory requirements, the present application constitutes a continuation-in-part of U.S. patent application Ser. No. 11/647,533, entitled COMPUTATIONAL SYSTEMS FOR BIOMEDICAL DATA, naming Edward K. Y. Jung; Royce A. Levien; Robert W. Lord and Lowell L. Wood, Jr. as inventors, filed 27 Dec. 2006 which is currently co-pending, or is an application of which a currently co-pending application is entitled to the benefit of the filing date.

**[0005]** The United States Patent Office (USPTO) has published a notice to the effect that the USPTO's computer programs require that patent applicants reference both a serial number and indicate whether an application is a continuation or continuation-in-part. Stephen G. Kunin, Benefit of Prior-Filed Application, USPTO Official Gazette Mar. 18, 2003, available at <http://www.uspto.gov/web/offices/com/sol/og/2003/week11/patbene.htm>. The present Applicant Entity (hereinafter "Applicant") has provided above a specific reference to the application(s) from which priority is being claimed as recited by statute. Applicant understands that the statute is unambiguous in its specific reference language and does not require either a serial number or any characterization, such as "continuation" or "continuation-in-part," for claiming priority to U.S. patent applications. Notwithstanding the foregoing, Applicant understands that the USPTO's computer programs have certain data entry requirements, and hence Applicant is

designating the present application as a continuation-in-part of its parent applications as set forth above, but expressly points out that such designations are not to be construed in any way as any type of commentary and/or admission as to whether or not the present application contains any new matter in addition to the matter of its parent application(s).

**[0006]** All subject matter of the Related Applications and of any and all parent, grandparent, great-grandparent, etc. applications of the Related Applications is incorporated herein by reference to the extent such subject matter is not inconsistent herewith.

### TECHNICAL FIELD

**[0007]** This description relates to data handling techniques.

### SUMMARY

**[0008]** An embodiment provides a method. In one implementation, the method includes but is not limited to accepting an input providing innate determinant data from at least one sample, accessing a dataset to identify, based on the innate determinant data, at least one innate allergy determinant in the at least one sample, accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information; and presenting a signal related to ingestion-dependent allergy predisposition information in response to accessing the allergy test dataset to identify, based on the at least one innate allergy determinant, the allergy predisposition information. In addition to the foregoing, other method aspects are described in the claims, drawings, and text forming a part of the present disclosure.

**[0009]** An embodiment provides a method. In one implementation, the method includes but is not limited to accepting an input providing innate determinant data from at least one sample at one or more user interfaces; and transmitting data from the one or more user interfaces to at least one data analysis system, the data including at least the innate determinant data; the data analysis system being capable of accessing a dataset to identify, based on the innate determinant data, at least one innate allergy determinant in the at least one sample; accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information; presenting a signal related to ingestion-dependent allergy predisposition information in response to accessing the allergy test dataset to identify, based on the at least one innate allergy determinant, the allergy predisposition information; and the data analysis system further being capable of sending a signal to either the one or more user interfaces or a different user interface in response to the allergy predisposition information, which signal transmits the ingestion-dependent allergy predisposition information. In addition to the foregoing, other method aspects are described in the claims, drawings, and text forming a part of the present disclosure.

**[0010]** An embodiment provides a method. In one implementation, the method includes but is not limited to accepting an input identifying at least one allergic reaction to an allergen, accessing a dataset to identify at least one innate allergy determinant of the at least one allergic reaction in a population, accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, a portion of the population with a predisposition to the allergic

reaction, calculating, based on the portion of the population with a predisposition to the allergic reaction, an allergic index for the population; and presenting a signal related to the allergic index for the population in response to calculating, based on the portion of the population with a predisposition to the allergic reaction, the allergic index for the population. In addition to the foregoing, other method aspects are described in the claims, drawings, and text forming a part of the present disclosure.

**[0011]** In one or more various aspects, related systems include but are not limited to circuitry and/or programming for effecting the herein-referenced method aspects; the circuitry and/or programming can be virtually any combination of hardware, software, and/or firmware configured to effect the herein-referenced method aspects depending upon the design choices of the system designer.

**[0012]** An embodiment provides a system. In one implementation, the system includes but is not limited to circuitry for accepting an input providing innate determinant data from at least one sample, circuitry for accessing a dataset to identify, based on the innate determinant data, at least one innate allergy determinant in the at least one sample, circuitry for accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information, and circuitry for presenting a signal related to ingestion-dependent allergy predisposition information in response to the allergy predisposition information. In addition to the foregoing, various other method and/or system and/or program product aspects are set forth and described in the teachings such as text (e.g., claims and/or detailed description) and/or drawings of the present disclosure.

**[0013]** An embodiment provides a system. In one implementation, the system includes but is not limited to circuitry for accepting an input providing innate determinant data from at least one sample at one or more user interfaces; and circuitry for transmitting data from the one or more user interfaces to at least one data analysis system, the data including at least the innate determinant data: the data analysis system being capable of accessing a dataset to identify, based on the innate determinant data, at least one innate allergy determinant in the at least one sample; accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information; presenting a signal related to ingestion-dependent allergy predisposition information in response to the allergy predisposition information; and the data analysis system further being capable of sending a signal to either the one or more user interfaces or a different user interface in response to the allergy predisposition information, which signal transmits the ingestion-dependent allergy predisposition information. In addition to the foregoing, various other method and/or system and/or program product aspects are set forth and described in the teachings such as text (e.g., claims and/or detailed description) and/or drawings of the present disclosure.

**[0014]** An embodiment provides a computer program product. In one implementation, the system includes but is not limited to a signal-bearing medium bearing (a) one or more instructions for accepting an input providing innate determinant data from at least one sample; (b) one or more instructions for accessing a dataset to identify, based on the innate determinant data, at least one innate allergy determinant in the at least one sample; (c) accessing an allergy test

dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information; and (d) one or more instructions for presenting a signal related to ingestion-dependent allergy predisposition information in response to accessing the allergy test dataset to identify, based on the at least one innate allergy determinant, the allergy predisposition information. In addition to the foregoing, various other method and/or system and/or program product aspects are set forth and described in the teachings such as text (e.g., claims and/or detailed description) and/or drawings of the present disclosure.

**[0015]** An embodiment provides a system. In one implementation, the system includes but is not limited to a computing device and instructions. The instructions when executed on the computing device cause the computing device to (a) accept an input providing innate determinant data from at least one sample; (b) access a dataset to identify, based on the innate determinant data, at least one innate allergy determinant in the at least one sample, (c) access an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information; and (d) present a signal related to ingestion-dependent allergy predisposition information in response to accessing the allergy test dataset to identify, based on the at least one innate allergy determinant, the allergy predisposition information. In addition to the foregoing, other system aspects are described in the claims, drawings, and text forming a part of the present disclosure.

**[0016]** In addition to the foregoing, various other method and/or system and/or program product aspects are set forth and described in the teachings such as text (e.g., claims and/or detailed description) and/or drawings of the present disclosure.

**[0017]** The foregoing is a summary and thus contains, by necessity, simplifications, generalizations and omissions of detail; consequently, those skilled in the art will appreciate that the summary is illustrative only and is NOT intended to be in any way limiting. Other aspects, features, and advantages of the devices and/or processes and/or other subject matter described herein will become apparent in the teachings set forth herein.

#### BRIEF DESCRIPTION OF THE DRAWINGS

**[0018]** With reference now to FIG. 1, shown is an example of a data analysis system in which embodiments may be implemented, perhaps in a device, that may serve as a context for introducing one or more processes and/or devices described herein.

**[0019]** FIG. 2 illustrates certain alternative embodiments of the data analysis system of FIG. 1.

**[0020]** FIG. 3 illustrates an embodiment of study data associated with the data analysis system of FIG. 1.

**[0021]** FIG. 4 illustrates alternative embodiment of study data associated with the data analysis system of FIG. 1.

**[0022]** FIG. 5 illustrates another alternative embodiment of study data associated with the data analysis system of FIG. 1, with specific examples of study data.

**[0023]** FIG. 6 illustrates additional alternative embodiments of study data associated with the data analysis system of FIG. 1, with specific examples of study data.

**[0024]** FIG. 7 illustrates additional alternative embodiments of study data associated with the data analysis system of FIG. 1, with specific examples of study data.

[0025] FIG. 8 illustrates additional alternative embodiments of study data associated with the data analysis system of FIG. 1, with specific examples of study data.

[0026] With reference now to FIG. 9, shown is an example of an operational flow representing example operations related to computational systems for biomedical data that may serve as a context for introducing one or more processes and/or devices described herein.

[0027] FIG. 10 illustrates an alternative embodiment of the example operational flow of FIG. 9.

[0028] FIG. 11 illustrates an alternative embodiment of the example operational flow of FIG. 9.

[0029] FIG. 12 illustrates an alternative embodiment of the example operational flow of FIG. 9.

[0030] FIG. 13 illustrates an alternative embodiment of the example operational flow of FIG. 9.

[0031] FIG. 14 illustrates an alternative embodiment of the example operational flow of FIG. 9.

[0032] FIG. 15 illustrates an alternative embodiment of the example operational flow of FIG. 9.

[0033] FIG. 16 illustrates an alternative embodiment of the example operational flow of FIG. 9.

[0034] With reference now to FIG. 17, shown is an example of an operational flow representing example operations related to computational systems for biomedical data that may serve as a context for introducing one or more processes and/or devices described herein.

[0035] With reference now to FIG. 18, shown is an example of an operational flow representing example operations related to computational systems for biomedical data that may serve as a context for introducing one or more processes and/or devices described herein.

[0036] With reference now to FIG. 19, shown is a partial view of an example computer program product that includes a computer program for executing a computer process on a computing device related to computational systems for biomedical data that may serve as a context for introducing one or more processes and/or devices described herein.

[0037] With reference now to FIG. 20, shown is an example device in which embodiments may be implemented related to computational systems for biomedical data that may serve as a context for introducing one or more processes and/or devices described herein.

[0038] The use of the same symbols in different drawings typically indicates similar or identical items.

#### DETAILED DESCRIPTION

[0039] FIG. 1 illustrates an example research system 100 in which embodiments may be implemented. The research system 100 includes an allergy data analysis system 102. The allergy data analysis system 102 may be used, for example, to store, recall, access, implement, or otherwise use datasets or other information obtained from study data 106.

[0040] The allergy data analysis system 102 may be used, for example, to determine allergy susceptibility in a population, including an individual, for a given allergy by analyzing innate (e.g., genetic) determinants and test (e.g., environmentally determined) data that together are associated with the allergy. The allergy data analysis system 102 may determine such susceptibility by, for example, storing, analyzing and/or providing information obtained from study data 106 as to the associations between allergy determinants and levels of allergy symptoms.

[0041] An allergy is typically an immune-mediated hypersensitivity to things in the environment. Allergies can cause, for example, skin irritation, respiratory distress, or, in extreme cases, anaphylactic shock and death. Examples of allergies include peanut allergy, pollen allergy, and asthma. Allergies are among the most common causes of chronic health problems in industrialized countries, affecting up to one third of the general population.

[0042] The Gell and Coombs classification divides allergies into four pathophysiological types, namely immediate (Type I, including anaphylaxis), antibody-mediated cytotoxic reactions (Type II), immune complex-mediated reactions (Type III), and delayed type hypersensitivity (Type IV). Although this classification was proposed more than 30 years ago, it is still widely used. There are, however, hypersensitivities that do not fit within the Gell and Coombs classification; at least three different situations can be identified in this vein, namely pseudo-allergic reactions, primarily antibody-mediated reactions and cell-mediated reactions, all of which are considered to be allergies as that term is used herein. Other hypersensitivities not included within the Gell and Coombs Type I-IV are to be considered allergies as that term is used herein. Similarly, the term "allergen," discussed below, includes agents that cause both Gell and Coombs Type I, II, III, and/or IV reactions, and/or other hypersensitivities.

[0043] Atopy defines a general predisposition to develop allergic reactions to otherwise innocuous substances. Atopic individuals may have serum IgE levels that are up to one-thousand fold higher than that of a normal individual.

[0044] Examples of known allergies include foreign proteins found in foreign serum from blood transfusions and vaccines, plant pollens (e.g., hay fever, rye grass, ragweed, timothy grass, and birch trees), mold spores, fungus, drugs (e.g., penicillins and other antibiotics, sulfonamides, salicylates (also found naturally in numerous fruits), NSAIDs, beta blockers, chemotherapeutics, anti-convulsants, and anesthetics), foods (e.g., nuts, sesame, seafood, egg (typically albumin, the egg white), peas, beans, peanuts, soybeans and other legumes, soy, milk, wheat, and corn), insect stings (e.g., bee sting venom, and wasp sting venom), animal products (e.g., animal hair and dander (e.g., dog, cat, horse, rabbit, hamster, guinea pig, gerbil, or bird), cockroach calyx, and dust mite excretion), chemical allergies (e.g., thimerosal, formaldehyde, phenol, sulfite, glycerin, hydrocarbon, pesticide, metal, fertilizer, or airborne pollutants), and latex.

[0045] Allergies are thought to be caused by environmental exposure to allergens. An allergen is any substance that is recognized by the immune system and causes an allergic reaction. Many allergen databases exist and are accessible to the public. Such databases include, for example, the web-based Structural Database of Allergenic Proteins (SDAP) permits the user to quickly compare the sequence and structure of allergenic proteins. Data from literature sources and previously existing lists of allergens are combined in a MySQL interactive database with a wide selection of bioinformatics applications. SDAP is available on the web at <http://fermi.utmb.edu/SDAP/index.html>.

[0046] Further, The International Union of Immunological Societies (IUIS) has published a list of allergens by source, taxonomic order, allergen name, isoallergen name (if present), common name, biochemical name, obsolete name, molecular weight by SDS-PAGE analysis, allergen allergenicity, allergen allergenicity literature reference, reference



and/or accession number(s), isoallergen allergenicity (if present), isoallergen allergenicity reference (if present), amino acid sequence, amino acid sequence reference, and sequence features. This list is updated annually and is available on the web at <http://www.allergen.org/Allergen.aspx>. Alternatively, the list is downloadable at the administration page of <http://www.allergen.org/Allergen.aspx> at the link "Download Excel readable version: ExportReadable.xls" on that page.

**[0047]** Allergy diagnosis is a crucial step in avoiding allergy problems. Allergies may develop in infants within a very short time after birth. For example, peanut allergy may be induced in an infant through the mother's diet during gestation or nursing. Current allergy diagnosis involves tests for immunoglobulin E (IgE), the antibody that is responsible for the allergic reaction. Such tests may measure total IgE levels and/or levels of IgE that recognize a specific allergen (specific IgE). Other allergy diagnostic tests involve skin tests using the allergen to elicit a skin reaction in allergic subjects.

**[0048]** One problem with current allergy diagnostic methods is a relatively poor clinical specificity; i.e., both positive in vitro IgE tests and positive skin tests are common in sensitized subjects who are asymptomatic. These false positives are common in food allergy cases, for example, where another diagnostic test, the food challenge, is sometimes used. Food challenges can be performed either in an open protocol or by double blind challenge. The gold standard for food allergy diagnosis is the double blind placebo-controlled food challenge. These studies are undertaken in a hospital where the patient receives a series of capsules or liquid containing either the food or placebo. Short-term elimination diets (2-3 weeks) can be helpful in some subjects. It is important that the food is totally eliminated as exposure to even small amounts of the food protein may lead to eczema. In the case of infants being breastfed, the mother may also need to eliminate the food from her diet. Some maternal food proteins have been shown to cross into breast milk.

**[0049]** One common IgE test is the RAST test (short for radioallergosorbent test). The RAST test, using a person's extracted blood, detects the amount of IgE that reacts specifically with suspected or known allergens. If a person exhibits a high level of IgE directed against pollen, the test may indicate the person is allergic to, e.g., pollen (or pollen-like) proteins. However, a person who has outgrown an allergy may still have a positive IgE test years after exposure. Many subjects with eczema have very high levels of total IgE; low-level false positive results may be seen in these cases because there is so much IgE present in the blood sample that it shows up as a positive result for allergens that the person is not allergic to. Similarly, allergens with similar protein structures may cross-react, resulting in false positive results. Also, the level of positivity of the test generally is not indicative of the degree of allergy present.

**[0050]** Commonly, diagnosis of food allergy relies on a significant clinical history of allergy symptoms plus evidence of specific IgE to the food allergen in question. The absence of a specific IgE to a food means that there is a 95% probability that the ingestion of the food will not lead to clinical symptoms. The presence of specific IgE to a particular food, however, has only at best a 50% positive predictive value when correlated with a positive food challenge.

**[0051]** Currently, two types of tests can help predict whether someone will have an allergic reaction to future bee stings. Neither test is perfect. Skin testing results correlate best with the magnitude of subsequent allergic reactions. Still, up to 46% of nonallergic individuals have positive skin tests and up to 25% of allergic individuals have negative skin tests.

**[0052]** Skin tests also are imperfect; some studies have shown that only 1/3 of positive food skin tests could be confirmed by a double blind food challenge. Other studies have shown that up to 46% of nonallergic individuals have positive skin tests. In addition, eliminating all foods to which the patient reacts to on skin testing may lead to nutritional problems.

**[0053]** As a result of such problems with current tests, improved diagnosis is needed. Recent studies have focused on biochemical events that are proximate to IgE recognition of allergens, such as histamine release by mast cells, as environmental markers for allergy. For example, Asero et al. have evaluated the potential of biological in vitro tests such as histamine release tests or basophil activation tests including assays performed with permanently growing cell lines (Asero et al., *Mol. Nutr. Food Res.*, 51(1), pp. 135-147 (2006)).

**[0054]** Beyond this, some groups have investigated possible genetic predictors of allergy. For example, it has been shown that the frequencies of two polymorphisms of the RANTES (a human chemokine) promoter region are significantly higher in subjects with allergic rhinitis than in control subjects. Others have looked at associations of human leukocyte antigen (HLA) gene polymorphisms with allergy. Twin studies have shown heritability estimates for eczema of 60% and it appears that a predisposition to atopic allergy may be heritable, although the specific form of allergy is generally not predictable based on a family history of atopy. Indeed, no genetic markers have been identified that can predict specific allergy susceptibility.

**[0055]** A sample, as used herein, may be, for example, any measurement of an individual's attribute, such as blood containing DNA for genetic analysis, or blood or other tissue for gene expression analysis.

**[0056]** An innate determinant, as used herein, may be, for example, a genetic sequence, including, for example, a single nucleotide polymorphism, haplotypes, and/or other gene sequence information. An innate determinant may also be, for example, gene expression information (e.g., mRNA expression information or protein expression information). An innate determinant may also be, for example, epigenetic information (e.g., DNA methylation, histone methylation, histone acetylation, histone phosphorylation, histone sumoylation, histone ubiquitylation/ADP-ribosylation, or regulatory short interfering RNA information), biochemical information such as liver cytochrome enzyme phenotype information, or specific cell population information. Alternatively, total IgE levels that are not associated with an allergy (e.g., an individual's normal, pre-exposure total IgE levels) may be the innate determinant.

**[0057]** For example, changes in histone acetylation at the IL-4 and IFN- $\gamma$  loci have been implicated in allergy susceptibility. (See Bousquet et al., "Epigenetic inheritance of fetal genes in allergic asthma," *Allergy*, vol. 59(2), pp. 138-147 (2004), which is incorporated by reference herein in its entirety).

[0058] Allergy test data, as used herein, may be, for example, a measure of sensitization to an allergen. For example, a measure of total IgE associated with the allergy may be the allergy test data, or a measure of specific IgE may be the allergy test data. Alternatively, for example, test datasets including sensitization to dietary, nutraceutical, or medical regimen information may be the allergy test data. Allergy skin tests, food challenge tests, and/or patch tests also may comprise the allergy test datasets.

[0059] Allergy predisposition information, including ingestion-dependent allergy predisposition information, may be, for example, a combination of innate allergy determinant and test allergy data together with associated allergy symptoms. Such allergy predisposition information may be reported in, for example, allergy studies and/or allergy databases. Allergy predisposition information provides an improved marker for individuals and/or groups of people that experience defined levels of allergy.

[0060] An agent, as used herein, may be, for example, a medical or non-medical intervention, including, for example, administration of prescription or non-prescription medications, small molecule drugs or biologics, nutraceuticals, or dietary supplements. An agent may also be, for example, alcohol or an illicit substance. An agent may be a prodrug or a metabolite of a compound.

[0061] As a further example, the allergy data analysis system 102 may, for a given agent associated with an allergic reaction, provide information about subpopulations for which the allergic reaction is acceptable or unacceptable within a defined limit relative to a general population. Identification of such subpopulations can provide avenues for agent testing and development according to defined levels of tolerance for an allergic reaction to an agent. On the basis of study data analysis, for example, for a given agent associated with an allergic reaction, a subpopulation exhibiting a specific level of allergy may be identified by accessing a dataset to identify at least one innate determinant of the allergic reaction in a population and to identify at least one allergy test determinant (e.g., IgE test result, skin test result, food challenge test result, etc.) of the allergic reaction in a population. Thus, identified subpopulations exhibit acceptable (or unacceptable, as specified) levels of allergy symptoms.

[0062] In FIG. 1, the allergy data analysis system 102 is used by a researcher 104. The researcher 104, for example, may use the allergy data analysis system 102 to enter, store, request, or access study data relating to innate allergy determinants, test data, and/or subject medical history data, such as, for example, the various examples provided herein. The researcher 104 may generally represent, for example, a person involved in health care or the health care industry, including, for example, a pharmaceutical company researcher or clinician, a biotechnology company researcher or clinician, a doctor, or a biomedical researcher. The researcher 104 also may represent someone who is involved in health care in the sense of developing, managing, or implementing the allergy data analysis system 102, e.g., a software developer with clinical knowledge (or access to clinical knowledge), a database manager, or an information technologies specialist. The researcher 104 also may represent a nutraceutical or cosmetics researcher. Even more generally, some or all of various functions or aspects described herein with respect to the researcher 104 may be performed automatically, e.g., by an appropriately-designed

and implemented computing device, or by software agents or other automated techniques.

[0063] Study data 106 is typically data relating to allergen, conditions of allergen ingestion or contact, allergy, allergy symptoms, subject attributes including genetic, gene expression, and biochemical characteristics, subject attributes including IgE levels, cell or enzyme phenotypes, subject medical history, allergy test data, statistical parameters and outcomes, and/or other experimental conditions or results. Study data 106 also may represent or include diagnostic testing, for example, to determine the effect of administration of an agent, such as a medication, on total or specific IgE levels.

[0064] Study data 106 may originate from, for example, an experiment and may be found in one or more different sources, including, for example, published journal articles, clinical trial reports including medical history data, data reported on internet site(s), data submitted to the Food and Drug Administration or other regulatory agency, data included in allergy and/or pharmacogenomic database(s), data included in genetic database(s), or data found in other relevant database(s) that contain data relating to allergic reactions to allergens, including the conditions of use, effect, mechanism of action or other properties of an allergen that are relevant to a subject. Study data 106 may also originate from a mathematical and/or computer simulation(s) of one or more properties of an agent, for example, data from an in vitro/in vivo correlation analysis. Study data 106, for example, could result from pre-clinical testing or clinical testing, and may include data from in vitro testing, in situ testing, in vivo testing in animals or clinical testing in human subjects. A formal clinical trial is one example of a study that results in study data 106.

[0065] Study data 106 may include raw data, for example, allergen or agent name, allergen concentration, allergen concentration in the blood at various times, and/or reported allergy symptoms experienced by study participants.

[0066] Study data 106 may also include study participant data or other information such as, for example, age, weight, gender, race, ethnicity, dietary factors, behavioral factors, medical history, concomitant medications, and other demographic characteristics. Study data 106 may also include molecular information about study participants such as, for example, genomic DNA sequence, cDNA sequence, single nucleotide polymorphisms (SNP's), haplotype profile, insertion and/or deletion (INDEL) profile, restriction fragment length polymorphism (RFLP) profile, chromatin state, nucleosome and/or histone/nucleoprotein composition, RNA sequence, micro RNA sequence, pyknon sequence and/or profile, RNA expression levels, protein sequence, protein expression levels, cytokine levels and/or activity, circulating hormone levels and/or activity, circulating carbohydrate levels, neurotransmitter levels, nitric oxide levels, liver enzyme expression and/or activity, gastrointestinal enzyme expression and/or activity, renal enzyme expression and/or activity, and/or other biochemical markers.

[0067] For example, data containing single-nucleotide polymorphisms in the ADAM33 gene (e.g., SNP ST+7) have been shown to be associated with asthma. (See Werner et al., "Asthma is associated with single-nucleotide polymorphisms in ADAM33," Clin. Exp. Allergy, vol. 34, pp. 26-31 (2004), which is incorporated by reference herein in its entirety).

**[0068]** Study data **106** may include data points that are, for example, ordinals (e.g., 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup>), nominals (e.g., itching, burning), binaries (e.g., alive/dead), genetic (e.g., AGCG-GAATTCA), and/or continuous (e.g., 1-4, 5-10).

**[0069]** As a further example, the allergy data analysis system **102** (including allergy data association logic **126** and/or allergy predisposition information logic **128**) may accept an input providing innate determinant data from at least one sample; access a dataset to identify, based on the innate determinant data, at least one innate allergy determinant in the at least one sample; access an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information; and present a signal related to ingestion-dependent allergy predisposition information in response to accessing the allergy test dataset to identify, based on the at least one innate allergy determinant, the allergy predisposition information. Study data **106** may report allergy levels, however it is understood that such reported data may or may not precisely match actual allergy levels.

**[0070]** The allergy data analysis system **102** also may associate innate allergy determinants and allergy test data with allergy symptoms (e.g., allergy predisposition information) with subpopulation identifier data to identify one or more relevant patient populations. For example, innate allergy determinants and allergy test data may be identified using the allergy data analysis system **102**, which determinants and data are associated with tolerable allergy levels in allergic or non-allergic individuals exposed to allergen. The allergy data analysis system **102** may then be used to further search, for example, one or more population databases to find subpopulation identifier data **312** (FIG. 3) that associate the innate and/or allergy test data with one or more relevant patient populations. Such population databases may include, for example, those that contain molecular information about individuals or populations such as, for example, genomic DNA sequence, cDNA sequence, single nucleotide polymorphisms (SNP's), haplotype profile, insertion and/or deletion (INDEL) profile, restriction fragment length polymorphism (RFLP) profile, chromatin state, nucleosome and/or histone/nucleoprotein composition, RNA sequence, micro RNA sequence, pyknon sequence and/or profile, RNA expression levels, protein sequence, protein expression levels, cytokine levels and/or activity, circulating hormone levels and/or activity, circulating carbohydrate levels, neurotransmitter levels, nitric oxide levels, liver enzyme expression and/or activity, gastrointestinal enzyme expression and/or activity, renal enzyme expression and/or activity, and/or other biochemical markers.

**[0071]** Ongoing, prospective and completed clinical trials for various allergies and agents may be found in databases such as <http://www.clinicaltrials.gov>, which lists specific details for clinical trials, including primary and secondary outcomes, enrollment size, inclusion and exclusion criteria, patient profiles, and other parameters. In addition, clinical trial results, including allergy trials, are generally available in journal publications that are known to, and accessible by, persons of ordinary skill in the art. As used herein, the terms data and dataset are interchangeable.

**[0072]** The allergy data analysis system **102** (including allergy data association logic **126** and/or allergy predisposition information logic **128**) may apply appropriate statistical methods to study data **106**, which may provide, for example, an average value(s) for a set of data, a confidence

level(s) for a confidence interval(s), p-value(s), or other measures of statistical significance for multiple data points in one or more datasets, such as observed or simulated study data **106**. Such statistical methods may comprise a query parameter that defines the level of the at least one allergy. For example, the allergy data analysis system **102** may include allergy data association logic **126** and/or allergy predisposition information logic **128** that is capable of applying a query parameter or statistical parameter to study data **106** as a means of identifying data and/or statistically significant data relevant to the associations between an innate allergy determinant and allergy test data, and allergy symptoms, or between allergy predisposition information (including ingestion-dependent allergy predisposition information) and a subpopulation.

**[0073]** Study data **106** relating to (1) associations of innate determinants with allergies; (2) associations of allergy test data with allergies; (3) associations of innate allergy determinants with allergies; and (4) associations of innate allergy determinants and allergy test data with allergy symptom information (e.g., allergy predisposition information) often are associated with a statistical measure of significance in terms of, for example, a statistical measure of association. For example, a particular HLA DNA sequence may be associated with an allergy predisposition to an extent that is statistically significant when compared to other HLA sequences. Further, the particular HLA DNA sequence accompanied by a certain level of total IgE in allergy patients may result in a statistically significant higher incidence of an allergy than is observed in populations having the particular HLA DNA sequence alone or the certain level of total IgE alone. Such combined innate allergy determinant data and allergy test data may have predictive effects for allergy susceptibility that are additive or even synergistic. Specificity of any association should be enhanced relative to analysis of innate or allergy test data alone, leading to fewer false positive and false negative allergy test results.

**[0074]** Statistical analysis may be classified into two main groups: hypothesis testing and estimation. In hypothesis testing, a study typically compares the occurrence of one or more endpoints in two or more groups of participants. This often involves a comparison of the mean, proportion, or other data parameter of, for example, allergy study data **304** (FIG. 3) in a test group to the same allergy study data **304** (FIG. 3) in a control group. Allergy study data **304** (FIG. 3), for example, may include measures such as mean levels of allergy symptoms associated with an innate and/or allergy test data. Allergy symptoms, for example, may include measures such as the mean incidence of anaphylaxis, or the proportion of subjects who experience breathing difficulty upon exposure to an allergen or other allergy trigger.

**[0075]** In estimation, the goal is to determine the relative value of a characteristic of interest in a group under study. The estimated value is usually accompanied by a statement about its certainty, or confidence interval, which is commonly expressed as a percentage. Estimation is important in hypothesis testing and in the analysis of safety variables. For example, in a study of a new antibiotic medication, the sponsor may be interested in estimating the proportion of patients that might experience a particular adverse event, including allergy symptoms. To ensure that the estimate has a high probability of being accurate, the allergy data analysis system **102** may determine the confidence interval for the estimate.

[0076] In the evaluation of study data, from whatever source, the character of the data is informative in terms of determining appropriate statistical measures to use to identify significant relationships and effects. The character of the data includes, for example, (1) the nature of the distribution of the primary, secondary, and influencing variables; (2) normal (Gaussian) or other well-known distributions; (3) if the data are not normally distributed, can they be changed by a function (e.g., a transformation) that preserves their order, but brings them into conformity with well-known assumptions about their distribution; (4) large enough sample size such that normality of the means can be assumed even if the data are not normally distributed; and/or (5) equality of variances of subgroups to be compared. These characteristics may be ascertained by applying common tests or by using basic data plots such as histograms or box plots. Knowing these characteristics of the data allows the allergy data analysis system 102 to validate the assumptions that underlie the data, and to select the most appropriate analytical method consistent with the data.

[0077] Study data 106 may, for example, contain two types of variables, quantitative and/or qualitative. Quantitative variables are numbers that may have, for example, a value within some acceptable range. For example, a person's blood pressure could be 120/80. Qualitative variables, however, typically lie within discrete classes, and are often characterized numerically by whole numbers. For instance, a subject who experiences nausea after agent administration could be characterized by a one, and a subject that does not could be classified as a zero. Qualitative variables may also be characterized by words.

[0078] The distribution of variables in a sample is important in determining what method of statistical analysis can be used. Normal, or Gaussian, distribution resembles the symmetrical bell-shaped curve by which most students are graded throughout their scholastic careers. It is typically characterized by two features: the mean, which is a measure of the location of the distribution, and the variance, which is a measure of the spread of the distribution. Many well-known statistical methods for analyzing means, such as the t-test or the paired t-test, rely on a normal distribution to ensure that the mean represents a measure of the center of the distribution.

[0079] Because statistical theory holds that the means of large samples are approximately normally distributed, an assumption of normality becomes less important as sample sizes increase. However, when sample sizes are small, it is important to determine whether the data to be analyzed are consistent with a normal distribution or with another well-characterized distribution.

[0080] Most common statistical tests of quantitative variables, including the t-tests and analysis of variance (ANOVA), are tests of the equality of the measures of location belonging to two or more subgroups that are assumed to have equal variance. A measure of location, such as a mean or median, is a single number that best describes the placement of the distribution (usually its center) on a number line. Because equal variance provides the basis of most tests that involve measures of location, in such cases an assumption of equal variance is more important than an assumption of normality, even when the tests do not rely on a specific distribution of the data (i.e., nonparametric tests). If the variances are not equal among the subgroups being compared, it is frequently possible to find a formula or

function (e.g., a transformation) that preserves order and results in variables that do have equal variance.

[0081] When considering the distribution of data, it is also useful to look at a picture of them. The allergy data analysis system 102 may plot data to determine whether the distribution is shifted toward higher or lower values (skewed). The presence of one or more values that are much higher or lower than the main body of data indicates possible outliers. Data plots can also help to locate other data peculiarities. Common, statistically sound adjustment methods known to those of skill in the art may be used to correct many types of data problems.

[0082] Once the character of the variables of interest has been established, the allergy data analysis system 102 can test for comparability between, for example, allergy and non-allergy control groups. Comparability is established by performing statistical tests to compare, for example, demographic factors, such as age at the time of the study, age at the time of allergy onset, nationality, economic status, migration status, and/or gender; or prognostic factors measured at baseline, such as allergy severity, concomitant medication, or prior therapies. Biased results can occur when the comparison groups show discrepancies or imbalances in variables that are known or suspected to affect primary or secondary outcome measures. For instance, when a group includes a large proportion of participants whose disease is less advanced than in those of a comparison group, the final statistical analysis will often show a more significant effect for the patients whose disease is less advanced, even though the effect may not be primarily caused by an administered agent.

[0083] For example, in a trial comparing the effectiveness of surgery and iodine-131 for treatment of hyperthyroidism, researchers found that, surprisingly, patients who received the allegedly less-traumatic radiation therapy had a much higher frequency of illness and death than those who underwent surgery. Examination of the baseline characteristics of the two groups revealed that the patients selected for the surgery group were generally younger and in better health than those selected for the iodine treatment. The inclusion criteria for the surgery group were more stringent than those for the iodine group because the patients had to be able to survive the surgery.

[0084] It is desirable to perform comparability tests using as many demographic or prognostic variables simultaneously as the method of analysis will allow. The reason for using this approach is that the influence of a single, for example, demographic or prognostic characteristic on an outcome variable may be strongly amplified or diminished by the simultaneous consideration of a second characteristic. However, the size of many clinical trials is often insufficient to allow the simultaneous consideration of more than two variables. More commonly, the sample size of the study will allow consideration of only one variable at a time.

[0085] Imbalances detected in comparability testing do not necessarily invalidate study results. By tracking such differences, however, the allergy data analysis system 102 can account for their presence when comparing study data from allergy and control groups. Many statistical procedures may be used to adjust for imbalances either before or during an analysis, but such adjustments should be limited to cases where the extent of the difference is relatively small, as judged by a person of ordinary skill in the art.

**[0086]** Methods used for comprehensive analysis of study data vary according to the nature of the data, but also according to whether the analysis focuses on the effectiveness or the safety of the allergen or agent. Selection of an appropriate statistical method should also take into account the nature of the allergen or agent under study. For example, in vitro diagnostic studies may use statistical techniques that are somewhat specialized. Often the analysis is based on a specimen, such as a vial of blood, collected from a patient. The same specimen is typically analyzed by two or more laboratory methods to detect an analyte, that is related to the presence of an allergy, condition or disease. Thus, each specimen results in a pair of measurements that are related to one another. The statistical treatment of such related (or associated) data is very different from that of unrelated (or un-associated) data because both measurements are attempting to measure exactly the same thing in the same individual. Generally, if both laboratory measurements result in a quantitative variable, a first statistical analysis will attempt to measure the degree of relationship between the measurements. The usual practice is to perform a simple linear regression analysis that assumes that the pairs of values resulting from the laboratory tests are related in a linear way.

**[0087]** In linear regression analysis, a best-fit line through the data is found statistically, and the slope is tested to determine whether it is statistically different from zero. A finding that the slope differs from zero indicates that the two variables are related, in which case the correlation coefficient, a measure of the closeness of the points to the best-fit line, becomes important. A correlation coefficient with a high value, either positive or negative, indicates a strong linear relationship between the two variables being compared. However, this correlation is an imperfect measure of the degree of relationship between the two measurements. That is, although a good correlation with a coefficient near one may not indicate good agreement between the two measurements, a low correlation is almost surely indicative of poor agreement.

**[0088]** Although correlation can indicate whether there is a linear relationship between two study measurements, it does not provide good information concerning their degree of equivalence. Perfect equivalence would be shown if the correlation were very near one, the slope very near one, and the intercept very near zero. It is possible to have a very good relationship between the two measures, but still have a slope that is statistically very different from one and an intercept that is very different from zero. In such a situation, one of the two measurements may be biased relative to the other.

**[0089]** Another relevant analysis of study data is a relative risk assessment or a receiver operating characteristic (ROC) analysis. Software is available to perform either of these analyses. A relative risk assessment is a ratio of the risk of a condition among patients with a positive test value to the risk of the condition among patients with a negative test value. The relative risk analysis can be done by use of either a logistic regression or a Cox regression depending on whether the patients have constant or variable follow-up, respectively. ROC analysis provides a measure of the robustness of the cutoff value as a function of sensitivity and specificity.

**[0090]** Analysis of the effectiveness and/or safety of an agent typically involves hypothesis testing to determine whether the agent maintains or improves the health of

patients in a safe way. In some cases, a particular agent may be compared to an agent of known function. In such cases, the result will be a test of the hypothesis that the unknown agent is better than or equal to the known agent. Selection of an appropriate statistical method for analysis of data from such studies depends on the answers to many questions, such as (1) is the primary variable quantitative or qualitative; (2) was the primary variable measured only once or on several occasions; (3) what other variables could affect the measurement under evaluation; and (4) are those other variables qualitative (ordered or not) or quantitative?

**[0091]** If the primary variable under evaluation is quantitative, selection of an appropriate method of analysis will depend on how many times that variable was measured and on the nature of any other variables that need to be considered. If there is only a single measurement for each variable, and there are no differences among the potential covariates belonging to the treated and control groups, the appropriate method of analysis may be a parametric or nonparametric ANOVA or t-test. For example, a safety study of a new antibiotic for allergic reaction incidence in healthy subjects, with all other things being equal, could compare 30 day allergy rates of incidence by this method.

**[0092]** The choice of an appropriate analytical method changes if the covariates belonging to the two comparison groups differ and are measured qualitatively. Such cases may use a more complex analysis of variance or an analysis of covariance (ANCOVA). The ANCOVA method is particularly suited to analyzing variables that are measured before and after treatment, assuming that the two measurements are related in a linear or approximately linear manner. Using ANCOVA, the researcher first adjusts the post-treatment measure for its relationship with the pre-treatment measure, and then performs an analysis of variance. Using the example of the antibiotic, ANCOVA would be a suitable method of analysis if the amount of allergic reaction incidence in subjects receiving the antibiotic depended, for example, on the patients' pre-treatment level of total IgE.

**[0093]** Outcome variables are often measured more than once for each study subject. When this is done, it should be done in a balanced way such that when a variable is measured it is measured for every subject. A balanced-repeated-measures ANOVA can be performed with or without covariates. With covariates, this method reveals the effect of each subject's covariate value on the outcome variable, the effect of time for each patient, and whether the effect of time for each patient is changed by different values of the covariate. Continuing with the antibiotic example, a repeated-measures ANOVA could be applied to evaluate measurements of allergy symptoms before antibiotic administration and at 3, 6, 9, and 12 days after initiation of dosing, and total IgE levels higher than, for example, 1000 ng/ml. In this case, the primary outcome variable is the level of allergy symptoms experienced, and the covariate is total IgE levels higher than 1000 ng/ml.

**[0094]** A repeated-measures ANOVA also may be used if a few patients missed a small number of measurements. However, in doing so the allergy data analysis system 102 may use other statistical algorithms known in the art in order to estimate the missing outcome measures.

**[0095]** Some studies result in a quantitative outcome variable and one or more quantitative covariates. In this situation, multiple regression methods are useful in evaluating outcome variables (called dependent variables), especially if

the study involves several levels or doses of exposure as well as other factors (independent variables). Regression is a powerful analytical technique that enables the allergy data analysis system 102 to simultaneously assess the primary variables as well as any covariates.

**[0096]** The regression model is an equation in which the primary outcome variable is represented as a function of the covariates and other independent variables. The importance of each independent variable is assessed by determining whether its corresponding coefficient is significantly different from zero. If the coefficient is statistically greater than zero, then that independent variable is considered to have an effect on the dependent variable and is kept in the model; otherwise, it is discarded. The final model includes only those variables found to be statistically related to the dependent variable. The model enables the allergy data analysis system 102 to determine the strength of each independent variable relative to the others, as well as to the allergen or agent effect. In the antibiotic example, a multiple regression analysis would be appropriate for data where the level of allergy symptoms was measured twice (e.g., at baseline and at 3 weeks), and the total IgE levels higher than 1000 ng/ml was measured as an independent variable.

**[0097]** For studies in which the outcome variable is qualitative, other types of analysis may be employed. Some of these resemble the methods used to analyze quantitative variables. For instance, log-linear modeling may be used to develop the same types of evaluations for a qualitative outcome variable as ANOVA and ANCOVA provide for quantitative measures.

**[0098]** Log-linear modeling techniques are equivalent to such commonly used Chi-square methods as the Cochran-Mantel-Haenszel method. They enable the allergy data analysis system 102 to compare the distribution of allergy and control patients within outcome classes; some techniques also make it possible to determine how consistent the influence of covariates is, and to adjust for that influence.

**[0099]** Because qualitative variables are represented by whole numbers, these methods may use special algorithms in order to estimate quantities of interest. Finding solutions for estimating those quantities can be accomplished readily with the aid of computer programs known in the art.

**[0100]** Logistic regression methods are the qualitative counterparts to the multiple regression techniques described for quantitative variables. While the two methods include models and interpretations that correspond closely, logistic regression computations are not as straightforward as those for multiple regression. Even so, they enable the allergy data analysis system 102 to determine relationships between the outcome variable and independent variables. Logistic regression allows the use of either quantitative or qualitative covariates, but it is preferred that study participants have a follow-up time that is essentially the same.

**[0101]** In logistic regression methods, a proportion is represented by a complex formula, a part of which is a multiple regression-like expression. By estimating the coefficients for the independent variables, including the allergen exposure or agent administration, the allergy data analysis system 102 is able to determine whether a particular independent variable is statistically related to the dependent variable. The final model contains only these independent variables, the coefficients of which differ significantly from zero. Further, the logistic regression method estimates the odds ratio: a measure of the relative risk for each indepen-

dent variable adjusted for the presence of the other variables. For example, if the allergen was a drug intended to treat a fungus on the toenail, and if the logistic regression measured the rate of allergy in treated subjects at 10 days after treatment, then an odds ratio of 7.9 for the treatment would imply that, adjusted for other variables in the final model, subjects who had the treatment were 7.9 times more likely to experience an allergic reaction at 10 days after treatment than patients who did not have the treatment.

**[0102]** The Cox regression method is another technique for analyzing qualitative outcome measures. This method can determine the effect of agents and other potential covariates even when the data do not have the same follow-up time. It yields a model and results that are analogous to those of the logistic regression method, but are not limited to patient survival outcomes. This method can be applied to, for example, an outcome that includes measurement of the time to a particular event, such as time to allergy symptom onset. A powerful characteristic of the Cox regression method is that it keeps the study participant in the analysis until he or she drops out of the study. This can be an important factor in small studies, in which statistical power can be reduced when even a modest number of participants are unavailable for follow-up.

**[0103]** The selection of statistical methods appropriate for safety analyses depends on many factors. If the FDA and the clinical researcher have a great deal of knowledge about adverse events, such as allergy symptoms for example, associated with a specific treatment target and/or its therapeutic agents, estimating the rate of adverse events with corresponding 95% confidence intervals may be appropriate. But if little is known about those adverse events, a more elaborate statistical treatment may be appropriate.

**[0104]** The most common method used to analyze adverse events is to compute freedom-from-complication rates by survival methods; one of the most commonly used analysis procedures for survival data is the Kaplan-Meier method. The popularity of this method is partly attributable to the fact that it measures the time to occurrence of an adverse event, and, like the Cox regression method, keeps participants in the life table until they drop out of a study. In addition, at the occurrence of each adverse event, the Kaplan-Meier method provides an estimate of the adverse event rate and its standard error, enabling the allergy data analysis system 102 to compute confidence intervals for each adverse event.

**[0105]** A related method is the life table method, in which the study duration is divided into equal segments and the proportion of events and participant drop-outs is evaluated for each segment. For example, if the study had a one-year duration, the life table could be viewed as 12 one-month segments. Calculation of rates would depend on the number of participants that entered the study each month, the number of events that occurred in that month, the number of participants that dropped out of the study in that month, and the number of participants who went on to the next month. The adverse event rate is calculated for each month rather than at the occurrence of each adverse event, and the standard error is also determined, allowing for the computation of confidence intervals.

**[0106]** If it is necessary to test the hypothesis that two samples (such as a control and exposed group) have the same adverse event experience for the study duration in the presence of covariates, this can be accomplished by comparing survival (freedom from complication) rates derived

through use of the Cochran-Mantel-Haenzel method or an equivalent procedure. Cox regression provides a good method with which to determine the relative importance of covariates on a rate of adverse events.

**[0107]** Such analytical methods are useful for comparing the rates at which a treated and control group encounter their first occurrence of an adverse event, but the occurrence of multiple adverse events or multiple occurrences of the same adverse event do not lend themselves readily to a single appropriate analytical technique. A combination of non-independent analyses is preferred to completely explain the effects of multiple adverse events.

**[0108]** Numerical relationships detected as statistically significant by regression techniques are associations, not cause-and-effect relationships. To support the associative evidence provided by such analyses, the allergy data analysis system **102** may also make use of pre-clinical animal studies and other data that reinforce the determination of cause-and-effect, where available.

**[0109]** While it is generally desirable to prospectively design a study to provide statistically significant measures of safety and efficacy, retrospective analysis of study data **106** may provide adequate means for determining statistical relationships among the data. Alternatively, statistically significant measures of study data **106** may be unavailable in some cases. For example, an analysis of study data **106** may indicate an association between the allergy symptoms of a small subset of allergic patients enrolled in a clinical trial and a specific set of innate and allergy test data (e.g., genetic and IgE data, respectively) of the small subset of allergic patients. Because of the small sample size of the subset of patients, the study data **106** may lack statistical power to indicate whether the association is statistically significant (e.g., the p-value may be  $>0.05$ ). The association, however, may nevertheless be of interest by virtue of, for example, (1) the degree of association; (2) the magnitude of the allergy symptoms in the subset of patients; and/or (3) a coincidence with a known mechanism of action of the innate determinant. Therefore, the claimed subject matter should not be limited to study data analysis of, for example, a specific statistical level of significance. Many applications of the allergy data analysis system **102** exist, over and above the examples provided herein.

**[0110]** Study data **106** may include reported or calculated mean values of the parameters discussed above such as, for example, arithmetic, geometric and/or harmonic means. Study data may also include reported or calculated statistical measures such as student's t-test, p-value, chi square value (s), and/or confidence interval or level. Alternatively, the allergy data analysis system **102** may calculate an appropriate statistical measure using raw data.

**[0111]** As discussed above, a query parameter may be applied to the study data **106** as a means of selecting desired, relevant, and/or statistically significant data. Such a query parameter may be accepted, for example, by the allergy data association logic **126** and/or allergy predisposition information logic **128** as input or associated with input from a researcher **104** through a user interface **132**.

**[0112]** In this regard, it should be understood that the herein claimed allergy data analysis system **102** can, for a given allergy, accept a query parameter that defines the level of the at least one allergy against which the association of accessed data including innate allergy determinants, allergy test data, and/or allergy symptoms and/or defined allergy

level (e.g., allergy predisposition information) is made before presenting a signal related to, e.g., ingestion-dependent allergy predisposition information in response to the allergy predisposition information.

**[0113]** For example, many databases may be searched singly or in combination to identify one or more allergies that are associated with innate determinants, such as for example, a specific HLA DNA sequence. Similarly, many databases exist that may be searched singly or in combination to identify data containing allergy test data associated with one or more allergies, such as total and/or specific IgE measurements, skin test results, and/or food challenge results. Similarly, many databases exist that may be searched singly or in combination to associate a given innate allergy determinant and a given allergy test dataset with the allergy. Similarly, many databases exist that may be searched singly or in combination to identify one or more subpopulations that correspond to populations with specific innate and/or allergy test data.

**[0114]** Some allergies have a genetic component and are more likely to occur among people who trace their ancestry to a particular geographic area. People in an ethnic group often share certain versions of their genes, called alleles, which have been passed down from common ancestors. If one of these shared alleles contains a mutation that predisposes the carrier to experience a specific allergy, that allergy may be more frequently seen in that particular ethnic group than in other groups that do not carry the allele with the mutation.

**[0115]** Examples of genetic conditions that are more common in particular ethnic groups are sickle cell anemia, which is more common in people of African, African-American, or Mediterranean heritage; and Tay-Sachs disease, which is more likely to occur among people of Ashkenazi (eastern and central European) Jewish or French Canadian ancestry.

**[0116]** Linkage disequilibrium (LD) is a term used in the field of population genetics for the non-random association of alleles at two or more genetic loci, not necessarily on the same chromosome. LD describes a situation in which some combinations of alleles or genetic markers occur more or less frequently in a population than would be expected from a random assortment of allelic sequences based on their frequencies. For example, in addition to having higher levels of genetic diversity, populations in Africa tend to have lower amounts of linkage disequilibrium than do populations outside Africa, partly because of the larger size of human populations in Africa over the course of human history and partly because the number of modern humans who left Africa to colonize the rest of the world appears to have been relatively low. In contrast, populations that have undergone dramatic size reductions or rapid expansions in the past and populations formed by the mixture of previously separate ancestral groups can have unusually high levels of linkage disequilibrium.

**[0117]** Databases that contain study data **106** relating to, for example, the genetic make-up of a population, allergy trial information, including subject information and allergy symptoms experienced, include, for example, those found on the internet at the Entrez websites of the National Center for Biotechnology Information (NCBI). NCBI databases are internally cross-referenced and include, for example, medical literature databases such as PubMed and Online Mendelian Inheritance in Man; nucleotide databases such as GenBank; protein databases such as SwissProt; genome



databases such as Refseq; and expression databases such as Gene Expression Omnibus (GEO). The uniform resource locator (URL) for the NCBI website is <http://www.ncbi.nlm.nih.gov>. Also useful are publication databases such as Medline and Embase.

**[0118]** Other databases include, for example, IMS Health databases of prescribing information and patient reporting information such as that contained in the National Disease and Therapeutic Index (NDTI) database, which provides a large survey of detailed information about the patterns and treatment of disease from the viewpoint of office-based physicians in the continental U.S. Also of use is the U.S. Food and Drug Administration's (FDA's) Adverse Event Reporting System (AERS) database. This database contains adverse drug reaction reports from manufacturers as required by FDA regulation. In addition, health care professionals and consumers send reports voluntarily through the MedWatch program. These reports become part of a database. The structure of this database is in compliance with the international safety reporting guidance issued by the International Conference on Harmonization. The FDA codes all reported adverse events using a standardized international terminology called MedDRA (the Medical Dictionary for Regulatory Activities). Among AERS system features are the on-screen review of reports, searching tools, and various output reports. Another adverse drug events database is DIOGENES®, a database consisting of two sub-files: Adverse Drug Reactions (ADR) and Adverse Event Reporting System (AERS). ADR records contain data regarding a single patient's experience with a drug or combination of drugs as reported to the FDA. Since 1969, the FDA has legally-mandated adverse drug reaction reports from pharmaceutical manufacturers and maintained them in their ADR system. In November 1997, the ADR database was replaced by the AERS. Other adverse event reporting databases include, for example, the Vaccine Adverse Event Reporting System (VAERS).

**[0119]** In one embodiment, the allergy data analysis system **102** carries out the method of accepting an input providing innate determinant data from at least one sample, accessing a dataset to identify, based on the innate determinant data, at least one innate allergy determinant in the at least one sample, accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information; and presenting a signal related to ingestion-dependent allergy predisposition information in response to accessing the allergy test dataset to identify, based on the at least one innate allergy determinant, the allergy predisposition information. In doing so, the allergy data analysis system **102** may identify allergy predisposition information (e.g., a specific combination of innate allergy determinant [i.e., one or more molecular parameters such as, for example, DNA sequence, protein sequence, and/or protein expression level] and allergy test data [i.e., environmentally-induced parameters such as, for example, specific IgE titers directed to an allergen]) that is associated with a defined level of the allergy (e.g., allergy symptom incidence or severity of a defined level).

**[0120]** Data associated with an individual sample, population or subpopulation, as described and claimed herein, refer generally to data regarding a human or animal population or a human or animal subpopulation. For example, data associated with a individual, population or subpopulation may be, for example, reported in the scientific literature,

self-reported, measured, reported in survey results, present in archival documentation, and/or anecdotal in nature.

**[0121]** Data characterized by, for example, one or more genetic profiles may not, at first glance, correspond to a known, clinically-defined segment of the global or a national population. The allergy data analysis system **102** may therefore perform the additional step of associating an innate allergy determinant with subpopulation identifier data to identify one or more relevant patient populations. As an example, study data **106** associated with a defined level of at least one allergy may be molecular data or other data specifically associated with individuals having known ethnic, gender, age or other demographic features. As a specific example, study data characterized by a specific DNA sequence and total IgE level resulting in severe allergic symptoms may be matched with an ethnic genomic DNA database(s) and/or other medical database(s) to identify an ethnic group in which the specific DNA sequence is more common than in the general population. Such an ethnic population may accordingly be identified as of increased risk or predisposition for the allergy, where the total IgE level complements the DNA sequence predictor in terms of predictive value.

**[0122]** Although many other examples are provided herein and with reference to the various figures, it should be understood that many types and instances of study data **106** may play a role in the use and application of the various concepts referenced above and described in more detail herein. The allergy data analysis system **102** may store study data **106** in a database **136** or other memory, for easy, convenient, and effective access by the researcher **104**.

**[0123]** The study data **106** may include, for example, not only clinical study data and/or corresponding allergy determinants, data, and/or information, but also various other parameters and/or characteristics related to subjects or patients who experience allergy or who have been exposed to an allergen, examples of which are provided herein. Through detailed storage, organization, processing, and use of the study data **106**, the researcher **104** may be assisted in identifying appropriate data, subpopulations, allergies, and/or agents, in order, for example, to identify individuals and/or populations with a predisposition for an allergy and/or that are at risk for an allergy, or that are without or relatively free of a predisposition to an allergy. Ordered assignment, processing, and/or storage of information within the study data **106**, as described herein, facilitates and/or enables such recall, access, and/or use of the study data **106**; by the researcher **104** in identifying (1) allergy predisposition information associated with an allergy, including data containing at least one innate determinant associated with at least one allergy and test data associated with the at least one allergy, (2) an agent associated with a defined level of at least one allergy, and/or (3) subpopulation identifier data associated with allergy predisposition information and/or an innate allergy determinant.

**[0124]** In the allergy data analysis system **102**, allergy data association logic **126** and/or allergy predisposition information logic **128** may be used to store, organize, access, search, process, recall, or otherwise use the information stored in the study data **106**. For example, the allergy data association logic **126** and/or allergy predisposition information logic **128** may access a database management system (DBMS) engine **130**, which may be operable to perform computing operations to insert or modify new data into/within the study



data **106**, perhaps in response to new research or findings, or in response to a preference of the researcher **104**. For example, if a new allergen is discovered to be a health threat to the general population, the researcher **104** may access the allergy data analysis system **102** and/or allergy data association logic **126** and/or allergy predisposition information logic **128** through a user interface **132**, in order to use the DBMS engine **130** to associate the new allergen with allergy predisposition information (including, for example, innate allergy data, allergy test data, and allergy symptom information) that is associated with an acceptable incidence (or unacceptable incidence) of the allergic reaction to the allergen or a closely related allergen (e.g., with a defined level).

[0125] As another example, if allergy predisposition information from a newly published allergy study, e.g., a clinical trial report, can be associated with a subpopulation that was not specifically identified in the clinical trial report by the trial sponsors, the allergy data analysis system **102**, allergy data association logic **126** and/or allergy predisposition information logic **128** may present the subpopulation together with a signal related to the allergy predisposition information to a user interface **132** in response to input optionally including a query parameter from a researcher **104**. Such identification may be performed by use of a query parameter that can select, for example, a defined allergy symptom severity limit or allergy predisposition value for an allergic reaction.

[0126] Similarly, in a case where a researcher **104** seeks, for example, to identify subject data that is associated with the presence or absence of allergy symptoms for a given allergy, the researcher **104** may access the user interface **132** to use the allergy data association logic **126** and/or allergy predisposition information logic **128**, and/or DBMS Engine **130** to enter innate determinant data that is associated with an innate allergy determinant and allergy test data from a particular individual and/or population, such that allergy predisposition diagnosis is enhanced for that population. For example, if a researcher **104** is interested in individuals or populations that are particularly susceptible to a specific allergy, then the researcher **104** may input a specific level of allergy predisposition or allergy symptom character as a query parameter via the user interface **132**, together with an innate determinant, in order to access an innate allergy determinant and allergy test data that are associated with, for example, particularly high levels of allergy symptoms. The allergy data analysis system **102**, including allergy data association logic **126** and/or allergy predisposition information logic **128**, can then link the innate allergy determinant and allergy test data to, in this example, the particularly high levels of allergy symptoms, thereby identifying the allergy predisposition information. The allergy data analysis system **102**, including allergy data association logic **126** and/or allergy predisposition information logic **128**, also can then link the innate allergy determinant and/or allergy test data and/or allergy predisposition information to human subpopulations by virtue of common innate allergy determinants and/or environmental/allergy test data, thereby identifying those subpopulations that are predisposed to experience the allergy in question. In such an example, a researcher **104** may input a query parameter that, for example, specifies a level of allergy symptom or a statistically-defined level of allergy symptom together with the innate determinant.

[0127] As another example, if a researcher **104** is interested in finding an agent for use in the context of a particular treatment target or class of targets (e.g., beta blockers, statins, etc.) that will not elicit an allergy upon administration, then the researcher **104** may search for study data **106**, allergy predisposition information **310** (FIG. 3), and/or subpopulations that are not associated with significant allergy symptoms in response to administration of the agent. The allergy data association logic **126** and/or allergy predisposition information logic **128** may interface with the DBMS engine **130** to obtain, from the study data **106**, data and/or subpopulations that are associated with an allergy symptom profile within a defined limit. In this case, once the data, allergy predisposition information, and/or subpopulation is identified, the allergy data analysis system **102** and/or allergy data association logic **126** and/or allergy predisposition information logic **128** may present a signal related to the allergy predisposition information (e.g., a positive or negative association, or the character of the association) and/or subpopulation to the user interface **132** and the researcher **104** as one(s) that meets the input criteria, including the query parameter.

[0128] Allergy symptoms may include, for example, rhinitis, conjunctivitis, vasoconstriction, runny nose, tearing eyes, burning or itching eyes, red eyes, swollen eyes, itching nose, mouth, throat, skin, or any other area, wheezing, coughing, difficulty breathing, hives (skin wheals, urticaria), skin rashes, stomach cramps, vomiting, diarrhea, and/or headache, as well as incidence rates and degrees of the above symptoms.

[0129] As a general matter, a researcher **104**, e.g., a pharmaceutical or nutraceutical scientist, or other biomedical scientist, may not be aware of currently available content of the study data **106**. Thus, the allergy data analysis system **102** and/or allergy data association logic **126** and/or allergy predisposition information logic **128** provides the researcher **104** with fast, accurate, current, and/or comprehensive allergy study information, and also provides techniques to ensure that the information remains accurate, current, and/or comprehensive, by allowing the addition and/or modification of the existing study data **106**, as new study information becomes available.

[0130] In FIG. 1, the allergy data analysis system **102** is illustrated as possibly being included within a research device **134**. The research device **134** may include, for example, a mobile computing device, such as a personal digital assistant (PDA), or a laptop computer. Of course, virtually any other computing device may be used to implement the allergy data analysis system **102**, such as, for example, a workstation, a desktop computer, a networked computer, a collection of servers and/or databases, or a tablet PC.

[0131] Additionally, not all of the allergy data analysis system **102** need be implemented on a single computing device. For example, the study data **106** may be stored on a remote computer, while the user interface **132** and/or allergy data association logic **126** and/or allergy predisposition information logic **128** are implemented on a local computer. Further, aspects of the allergy data analysis system **102** may be implemented in different combinations and implementations than that shown in FIG. 1. For example, functionality of the DBMS engine **130** may be incorporated into the allergy data association logic **126** and/or allergy predisposition information logic **128**, and/or the study data **106**.

Allergy data association logic **126** and/or allergy predisposition information logic **128** may include, for example, fuzzy logic and/or traditional logic steps. Further, many methods of searching databases known in the art may be used, including, for example, unsupervised pattern discovery methods, coincidence detection methods, and/or entity relationship modeling.

[0132] The study data **106** may be stored in virtually any type of memory that is able to store and/or provide access to information in, for example, a one-to-many, many-to-one, and/or many-to-many relationship. Such a memory may include, for example, a relational database and/or an object-oriented database, examples of which are provided in more detail herein.

[0133] FIG. 2 illustrates certain alternative embodiments of the research system **100** of FIG. 1. In FIG. 2, the researcher **104** uses the user interface **132** to interact with the allergy data analysis system **102** deployed on the research device **134**. The research device **134** may be in communication over a network **202** with a data management system **204**, which also may be running the allergy data analysis system **102**; the data management system **204** may be interacted with by a data manager **206** through a user interface **208**. Of course, it should be understood that there may be many researchers other than the specifically-illustrated researcher **104**, each with access to an individual implementation of the allergy data analysis system **102**. Similarly, multiple data management systems **204** may be implemented.

[0134] In this way, the researcher **104**, who may be operating in the field, e.g., in an office, laboratory and/or hospital environment, may be relieved of a responsibility to update or manage content of the study data **106**, or other aspects of the allergy data analysis system **102**. For example, the data management system **204** may be a centralized system that manages a central database of the study data **106**, and/or that deploys or supplies updated information from such a central database to the research device **134**.

[0135] FIG. 3 illustrates an alternative embodiment of the study data **106** associated with the research system **100** of FIG. 1. In FIG. 3, and in the various examples herein, a particular nomenclature is used for the terms described above and related terms, in order to provide consistency and clarity of description. However, it should be understood that other terminology may be used to refer to the same or similar concepts.

[0136] In FIG. 3, innate determinant data **302** (e.g., **302a**, **302b**, **302c**, etc.) are stored and organized with respect to a plurality of allergy study data **304**. The allergy study data **304** include many of the terms and concepts just described, as well as additional, but not exhaustive, terms and concepts that may be relevant to the use and operation of the allergy data analysis system **102**.

[0137] For example, the allergy study data **304** may include innate allergy data **306**, also referred to as an innate allergy determinant. Innate allergy data **306** may refer to, for example, genetic or other personal characteristics data associated with allergy that are essentially independent of environmental exposure and sensitization to allergens. For example, innate allergy data **306** may include an eotaxin gene polymorphism that is found, in its homozygous form, at a high frequency in patients with asthma (see U.S. Pat. No. 6,548,245).

[0138] Allergy study data **304** also may include allergy test data **308**, also referred to as a test determinant associated with at least one allergy. Test allergy data **308** may refer to, for example, essentially environmentally-dependent personal characteristics associated with allergy, such as increased total IgE levels, levels of specific IgE directed to an allergen, a positive reaction to an allergy skin test or results of an allergy food challenge.

[0139] Allergy predisposition information **310** may refer, for example, to data reflecting the association of a particular combination of one or more innate allergy determinants and allergy test data with allergy symptoms, for example, as reported in allergy studies. Allergy predisposition information **310** may include, for example, innate allergy determinant and allergy test data associated with a defined level of incidence of nausea or abdominal pain following ingestion of, or skin exposure to, an allergen. One example of allergy predisposition information is ingestion-dependent allergy predisposition information **310b**. Ingestion-dependent allergy predisposition information **310b** is allergy predisposition information that relates to the association of innate allergy determinant and allergy test data with allergy symptoms resulting from the ingestion of at least one allergen.

[0140] Allergy study data **304** may also include subpopulation identifier data **312**. Subpopulation identifier data **312** may refer, for example, to data that tends to distinguish one subpopulation from other subpopulations or a general population, other than innate allergy data **306** in a specific case. Subpopulation identifier data **312**, for example, may include a genomic DNA sequence that is specific to a subpopulation and which tends to distinguish that subpopulation from other subpopulations or a general population. Subpopulation identifier data **312** may correlate with innate allergy data **306** and further characterize innate allergy data **306** in terms of readily recognizable populations (e.g., ethnic groups, blue-eyed people, or women, etc.).

[0141] In an alternative embodiment, innate allergy data **306** may be used as a query parameter to search one or more databases to identify subpopulation identifier data **312** that are associated with the innate allergy data **306**. Such subpopulation identifier data **312** may indicate clinically relevant subpopulation(s) for the allergy of interest. For example, using the allergy data analysis system **102** and/or agent identifier logic **126** and/or subpopulation identifier logic **128**, an allergy may be identified that is found with a particular frequency in a subpopulation characterized by, for example, a specific haplotype profile. That specific haplotype profile may then be used as a search parameter to search biomedical databases for prospective patient populations that are associated with the specific haplotype profile, e.g., individuals with primarily Mediterranean ancestry. The allergy data analysis system **102** and/or agent identifier logic **126** and/or subpopulation identifier logic **128** may subsequently access allergy test data **308** that, with the innate allergy determinant (i.e., innate allergy data **306**), comprise allergy predisposition information associated with a defined allergy level, thereby forming a relation to the subpopulation identifier data **312**-identified prospective patient population in terms of allergy susceptibility or resistance (e.g., individuals with primarily Mediterranean ancestry).

[0142] Many other examples of relationships and associations between the various allergy study data **304** and/or the innate determinant data **302** may be defined or determined and stored in the study data **106** according to the allergy data

association logic 126 and/or the allergy data association logic 126 and/or allergy predisposition information logic 128. Certain of these examples are provided herein.

[0143] Additionally, although the study data 106 is illustrated conceptually in FIG. 3 as a flat table in which one or more of the selected innate determinant data 302 are associated with one or more of the allergy study data 304, it should be understood that this illustration is for explanation and example only, and is not intended to be limiting in any way with respect to the various ways in which the study data 106 may be stored, organized, accessed, queried, processed, recalled, or otherwise used.

[0144] For example, the study data 106 may be organized into one or more relational databases. In this case, for example, the study data 106 may be stored in one or more tables, and the tables may be joined and/or cross-referenced in order to allow efficient access to the information contained therein. Thus, the innate determinant data 302 may define a record of the database(s) that are associated with various ones of the allergy study data 304.

[0145] In such cases, the various tables may be normalized so as, for example, to reduce or eliminate data anomalies. For example, the tables may be normalized to avoid update anomalies (in which the same information would need to be changed in multiple records, and which may be particularly problematic when database 136 is large), deletion anomalies (in which deletion of a desired field or datum necessarily but undesirably results in deletion of a related datum), and/or insertion anomalies (in which insertion of a row in a table creates an inconsistency with another row(s)). During normalization, an overall schema of the database 136 may be analyzed to determine issues such as, for example, the various anomalies just referenced, and then the schema is decomposed into smaller, related schemas that do not have such anomalies or other faults. Such normalization processes may be dependent on, for example, desired schema(s) or relations between the innate determinant data 302 and/or allergy study data 304, and/or desired uses of the study data 106.

[0146] Uniqueness of any one record in a relational database holding the study data 106 may be ensured by providing or selecting a column of each table that has a unique value within the relational database as a whole. Such unique values may be known as primary keys. These primary keys serve not only as the basis for ensuring uniqueness of each row (e.g., allergy) in the database, but also as the basis for relating or associating the various tables within one another. In the latter regard, when a field in one of the relational tables matches a primary key in another relational table, then the field may be referred to a foreign key, and such a foreign key may be used to match, join, or otherwise associate (aspects of) the two or more related tables.

[0147] FIG. 3 and associated potential relational databases represent only one example of how the study data may be stored, organized, accessed, recalled, or otherwise used.

[0148] FIG. 4 illustrates another alternative embodiment of study data 106 associated with the research system 100 of FIG. 1, in which the study data 106 is conceptually illustrated as being stored in an object-oriented database.

[0149] In such an object-oriented database, the various innate determinant data 302 and/or allergy study data 304 may be related to one another using, for example, links or pointers to one another. FIG. 4 illustrates a conceptualization of such a database structure in which the various types of

study data are interconnected, and is not necessarily intended to represent an actual implementation of an organization of the study data 106.

[0150] The concepts described above may be implemented in the context of the object-oriented database of FIG. 4. For example, the innate determinant data 302 may be associated with innate allergy data 306 and allergy test data 308. Innate determinant data 302 may be associated with data corresponding to an innate allergy determinant 306 and/or allergy test data 308. For example, innate determinant data 302 may be associated with innate allergy data 306, allergy test data 308 and allergy predisposition information 310 indicating a predisposition for the allergy.

[0151] Similarly, allergy predisposition information 310 may be associated with subpopulation identifier data 312. For example, allergy predisposition information 310 associated with innate determinant data 302 may be associated with subpopulation identifier data 312.

[0152] Many other examples of databases and database structures also may be used. Other such examples include hierarchical models (in which data is organized in a tree and/or parent-child node structure), network models (based on set theory, and in which multi-parent structures per child node are supported), or object/relational models (combining the relational model with the object-oriented model).

[0153] Still other examples include various types of eXtensible Mark-up Language (XML) databases. For example, a database may be included that holds data in some format other than XML, but that is associated with an XML interface for accessing the database using XML. As another example, a database may store XML data directly. Additionally, or alternatively, virtually any semi-structured database may be used, so that context may be provided to/as-associated with stored data elements (either encoded with the data elements, or encoded externally to the data elements), so that data storage and/or access may be facilitated.

[0154] Such databases, and/or other memory storage techniques, may be written and/or implemented using various programming or coding languages. For example, object-oriented database management systems may be written in programming languages such as, for example, C++ or Java. Relational and/or object/relational models may make use of database languages, such as, for example, the structured query language (SQL), which may be used, for example, for interactive queries for information and/or for gathering and/or compiling data from the relational database(s).

[0155] As referenced herein, the allergy data analysis system 102 and/or allergy data association logic 126 and/or allergy predisposition information logic 128 may be used to perform various data querying and/or recall techniques with respect to the study data 106, in order to facilitate determination of suitable allergy predisposition information 310. For example, where the study data 106 is organized, keyed to, and/or otherwise accessible using one or more of the innate determinant data 302 and/or allergy study data 304, various Boolean, statistical, and/or semi-boolean searching techniques may be performed.

[0156] For example, SQL or SQL-like operations over one or more of the innate determinant data 302 and/or allergy study data 304 may be performed, or Boolean operations using the innate determinant data 302 and/or allergy study data 304 may be performed. For example, weighted Boolean operations may be performed in which different weights or priorities are assigned to one or more of the innate deter-

minant data 302 and/or allergy study data 304, perhaps relative to one another. For example, a number-weighted, exclusive-OR operation may be performed to request specific weightings of desired or undesired study data to be included or excluded.

[0157] The researcher 104 may input a portion of an individual's genetic sequence as the innate determinant data 302, with the goal of identifying innate allergy data 306 and allergy predisposition information 310 that includes examples of innate allergy data 306 that belong to a particular class, for example, HLA, cytokine, or immunoglobulin gene sequence determinants. For example, the researcher 104 may want to identify allergy predisposition information 310 that is associated with a certain class of innate determinant data 302 and/or a certain class of allergy test data 308, e.g., statistically significant raised total IgE levels in allergic individuals. Having identified a set of innate allergy data 306 and/or allergy test data 308 meeting these criteria, the researcher 104 could then use the allergy data analysis system 102 to search relevant study data 106 using a query parameter such as a specific level of bronchoconstriction to identify allergy predisposition information 310 associated with, for example, acceptable levels of bronchoconstriction. In another example, the researcher 104 may specify relatively low levels of allergy incidence combined with a high degree of allergy symptom severity in an attempt to identify allergy predisposition information 310 corresponding to individuals with a high acute risk of allergy. Such a screen may identify allergy predisposition among various subpopulations for which desired allergy predisposition information is available.

[0158] As another example, the researcher 104 may start with a specific individual or subpopulation, characterized by either subpopulation identifier data 312 or innate allergy data 306, and proceed to identify allergy predisposition information 310 associated with an allergy that is, for example, not associated with significant predisposition for experiencing allergy symptoms in that individual or subpopulation.

[0159] The researcher 104 may specify such factors as subpopulation identifier data 312 or innate allergy data 306 as query parameters, using, for example, the user interface 132. For example, the researcher 104 may designate one or more of the innate determinant data 302/allergy study data 304, and assign a weight or importance thereto, using, for example, a provided ranking system. In this regard, and as referenced herein, it should be understood that the researcher 104 may wish to find particular groups of individuals at increased risk for a drug allergy, e.g., codeine allergy. The researcher 104 may not be aware of a subpopulation(s) of prospective patients that may be at increased risk for codeine allergy. However, the researcher 104 may query the allergy data analysis system 102 based on the desired innate determinant data 302, access innate allergy data 306 and allergy test data 308, and may thereby discover allergy predisposition information 310 corresponding to one or more groups that are particularly susceptible to, for example, codeine allergy. The researcher 104 may further query the allergy data analysis system 102 based on the innate allergy data 306 (i.e., part of the allergy predisposition information 310) to elicit subpopulation identifier data 312 that describe one or more clinically relevant prospective patient subpopulations at risk for codeine allergy.

[0160] Similarly, data analysis techniques (e.g., data searching) may be performed using the study data 106, perhaps over a large number of databases. For example, the researcher 104 may input a DNA sequence of interest. Then, the researcher 104 may receive a listing of allergy predisposition information ranked according to some input criteria. For example, the researcher 104 may receive a listing of instances of allergy predisposition information 310, ordered by allergy symptom severity, incidence of a particular allergy symptom in a general population, and incidence of a particular allergy in a subpopulation having innate allergy data 306 and allergy test data 308. In this way, for example, if a defined level of allergy symptom severity is a query parameter input provided by the researcher 104, then the researcher 104 may select allergy predisposition information 310 according to ranked allergy symptom severity.

[0161] By way of further example, other parameters/characteristics may be factored in. For example, elimination pathways may be tracked, databased, and/or weighted for use in the study data 106 and/or the allergy data analysis system 102. For example, if a particular allergen is typically eliminated by the liver before sensitization, then, in a case where allergy predisposition information 310 is identified that is characterized by allergy symptoms in individuals with compromised liver function (in terms of, e.g., innate allergy data 306 and allergy test data 308), such allergy predisposition information 310 may be used to provide an allergy risk warning to individuals with compromised liver function with respect to ingestion of the particular allergen. Algorithms implementing such query/recall/access/searching techniques may thus use Boolean or other techniques to output, for example, a thresholded, rank-ordered list. The allergy data association logic 126 and/or allergy predisposition information logic 128 may then assign a key or other identifier to such a list(s), for easier use thereof the next time a like query is performed.

[0162] Design and testing of querying techniques in particular implementations of the allergy data analysis system 102 may involve, for example, entry of candidate innate determinant data 302/allergy study-data 304 (or instances thereof) into a database(s), along with associated test results and/or affinity metrics that may be used to determine/weight targets or sets of targets. Then, an identifier may be generated that is unique to the treatment target set(s).

[0163] FIG. 5 illustrates another alternative embodiment of study data 106 associated with the research system 100 of FIG. 1, with specific examples of innate determinant data 302 and allergy study data 304. In particular, FIG. 5 provides or refers to example results from a related technical paper, which is specifically referenced below.

[0164] For example, the first through fourth rows of the table of FIG. 5 (i.e., rows 502, 504, 506, and 508, respectively) refer to examples that may be found in Eder et al., "Association between exposure to farming, allergies and genetic variation in CARD4/NOD1," *Allergy*, vol. 61, pp. 1117-24 (2006), which is hereby incorporated by reference in its entirety, and which may be referred to herein as the Eder reference.

[0165] In the Eder reference, data are reported for allergies to various inhaled allergens among children genotyped for a particular gene sequence, CARD4/NOD1. Eder et al. studied the association of asthma, hay fever, and allergen-specific serum IgE with exposure to a farming environment and with levels of endotoxin and muramic acid measured in house

dust samples. For example, the association of pollen-specific IgE levels in children with a specific CARD4/NOD1 genotype was associated with farm life, and with the lower and upper 50<sup>th</sup> percentile of exposure to endotoxin in the environment. The association provided a basis for calculating an odds ratio as a measure of the event frequency, i.e., what frequency of children with a specific genotype and specific pollen IgE level were raised on a farm or not raised on a farm.

[0166] Rows 502, 504, 506, and 508 represent fields of data reported for various CARD4/NOD1 genotypes. The Eder reference examined 668 children for their CARD4/NOD1 genotype and defined allergy to pollen, house dust mite, and cat dander as a serum specific IgE level for each allergen  $\geq 3.5$  IU/ml. Hay fever allergy was defined in children whose parents reported a doctor's diagnosis of hay fever in their child. The proportions of children with asthma, hay fever, and atopic sensitization were compared between farmer's and nonfarmer's children within the genotypes for the CARD4/NOD1 polymorphisms using the chi-squared test and the Fisher's exact test, respectively. Mantel Haenszel odds ratios for the association between farming and phenotype were computed and tested for homogeneity across genotypes. When a univariate test was suggestive, ( $P < 0.2$ ) of an association, a logistic regression model was used to control for potential confounders. When using logistic regression models, the log likelihood ratio test was applied to test for interaction between exposure and genotypes. The role of exposure to endotoxin and to levels of muramic acid concentrations in the association between CARD4/NOD1 genotypes and asthma and allergies was assessed in a similar manner.

[0167] As shown in row 502, allergy predisposition information 310 is present in the form of a 5.8% frequency of farmers' children having the CARD4/-21596 "TT" polymorphism (innate determinant data 502), and a specific pollen IgE level  $\geq 3.5$  and a farm upbringing (allergy test data 308). As a result of this study, the CARD4/-21596 "TT" polymorphism can be identified by the allergy data analysis system 102 by retrieving the association between genotype and allergy identified in the Eder reference. A calculated and reported 0.26 odds ratio for farmers' children having the CARD4/-21596 "TT" polymorphism and a specific pollen IgE level  $\geq 3.5$  relative to nonfarmers' children is also allergy predisposition information 310 for the CARD4/-21596 "TT" polymorphism 502. Thus, the odds ratio for the group with the specific innate allergy determinant and allergy test data is allergy predisposition information that gives an indication of differential allergy frequency for that group relative to other groups.

[0168] As shown in row 504, allergy predisposition information 310 is present in the form of a 14.3% frequency of farmers' children having the CARD4/-21596 "CC/CT" polymorphism (innate determinant data 504 and innate allergy data 306), and a specific house dust mite IgE level  $\geq 3.5$  and a farm upbringing (allergy test data 308). A calculated and reported 2.05 odds ratio for farmers' children having the CARD4/-21596 "CC/CT" polymorphism and a specific house dust mite IgE level  $\geq 3.5$  relative to nonfarmers' children is also allergy predisposition information 310 for dust mite allergy 504. Thus, the odds ratio for the group with the specific innate allergy data 306 and allergy test data

308 is allergy predisposition information 310 that gives an indication of differential allergy frequency for that group relative to other groups.

[0169] As shown in row 506, allergy predisposition information 310 is present in the form of a 0.0% frequency of farmers' children having the CARD4/-21596 "TT" polymorphism (innate determinant data 506 and innate allergy data 306), and a specific cat dander IgE level  $\geq 3.5$  and a farm upbringing (allergy test data 308). A calculated and reported 0.0 odds ratio for farmers' children having the CARD4/-21596 "TT" polymorphism and a specific cat dander IgE level  $\geq 3.5$  relative to nonfarmers' children is also allergy predisposition information 310 for cat dander allergy 506. Thus, the odds ratio for the group with the specific innate and allergy test data is allergy predisposition information that gives an indication of differential allergy frequency for that group relative to other groups.

[0170] As shown in row 508, allergy predisposition information 310 is present in the form of a 1.7% frequency of farmer's children having the CARD4/-21596 "TT" polymorphism (innate determinant data 508 and innate allergy data 306), and a doctor's hay fever diagnosis and a farm upbringing (allergy test data 308). A calculated and reported 0.11 odds ratio for farmers' children having the CARD4/-21596 "TT" polymorphism and a doctor's hay fever diagnosis relative to nonfarmers' children is also allergy predisposition information 310 for hay fever allergy 508. Thus, the odds ratio for the group with the specific innate and allergy test data is allergy predisposition information that gives an indication of differential allergy frequency for that group relative to other groups.

[0171] FIG. 6 illustrates another alternative embodiment of study data 106 associated with the research system 100 of FIG. 1, with specific examples of allergy study data 304. In particular, FIG. 6 provides or refers to example results from a related technical paper, which is specifically referenced below.

[0172] For example, the first and second rows of the table of FIG. 6 (i.e., rows 602 and 604, respectively) refer to examples that may be found in Yang et al., "HLA-DRB genotype and specific IgE responses in patients with allergies to penicillins," *Chin. Med. J.*, vol. 119(6), pp. 458-66 (2006), which is hereby incorporated by reference in its entirety, and which may be referred to herein as the Yang reference.

[0173] In the Yang reference, data are reported for allergies to penicillins among 113 allergy patients genotyped for particular HLA-DRB alleles. The Yang reference investigated the relationship between HLA-DRB genotype and allergies to various penicillins. For example, a significantly increased frequency of the DR9 allele was found in 77 patients with allergic reaction, and the same was true in those with immediate reaction and urticaria, respectively ( $p=0.011$ ;  $p=0.019$ ;  $p=0.005$ , respectively), and a significantly decreased frequency of the DR14.1 allele was found in 80 patients with positive IgE antibodies, with immediate reaction and with urticaria compared with control subjects ( $p=0.024$ ,  $p=0.038$ ;  $p=0.038$ , respectively).

[0174] Rows 602 and 604 represent fields of data reported for allergies to penicillin. The Yang reference examined 113 allergy patients and 87 healthy subjects for their HLA-DRB alleles. Of the 113 allergy patients genotyped, 35 had positive skin test as well as specific IgE antibodies. Significance of the observed associations was evaluated using

chi-square or Fisher's exact test if any value in a 2x2 table was less than 5. A p-value of less than 0.05 was considered statistically significant.

[0175] Rows **602** and **604** contain study data from the Yang reference, showing allergy study data. As shown in row **602**, innate determinant data **602** and innate allergy data **306** was identified in terms of the HLA DR9 genotype. Allergy test data **308** was also identified in terms of patients with specific penicillin IgE antibodies. Allergy predisposition information **310** is present in the form of 11.04% of HLA DR9 patients with allergic reaction; 6.25% of HLA DR9 patients with positive penicillin IgE antibodies; 12.16% of HLA DR9 patients with immediate reaction; and 13.51% of HLA DR9 patients with urticaria (compared to 4.02% of control subjects with an HLA DR9 allele). Thus, the specific innate allergy determinant (innate allergy data **306**) and allergy test data **308** among patients experiencing penicillin allergy is allergy predisposition information **310** that gives an indication of differential allergy frequency for that group relative to other groups.

[0176] As shown in row **604**, innate determinant data **604** and innate allergy data **306** was identified in terms of the HLA DR14.1 allele genotype. Allergy test data **308** was also identified in terms of patients positive for penicillin-specific IgE antibodies. Allergy predisposition information **310** is present in the form of 0% of HLA DR14.1, penicillin IgE-positive patients with an immediate reaction; and 0% of HLA DR14.1, penicillin IgE-positive patients with urticaria (compared to 9.77% of control subjects with an HLA DR14.1 allele). Thus, the specific innate allergy determinant (innate allergy data **306**) and allergy test data **308** among patients experiencing penicillin allergy is allergy predisposition information **310** that gives an indication of differential allergy frequency for that group relative to other groups.

[0177] FIG. 7 illustrates alternative embodiments of study data **106** associated with the research system **100** of FIG. 1, with specific examples of allergy study data **304**. In particular, FIG. 7 provides or refers to an example from a related technical paper, which is specifically referenced below.

[0178] For example, FIG. 7 refers to examples that may be found in Kalayci et al., "ALOX5 promoter genotype, asthma severity and LTC<sub>4</sub> production by eosinophils," *Allergy*, vol. 61, pp. 97-103 (2006), which is hereby incorporated by reference in its entirety, and which may be referred to herein as the Kalayci reference.

[0179] In the Kalayci reference, data are reported relating to the relationship between ALOX5 gene variants and asthma severity. The Kalayci reference genotyped the ALOX5 core promoter of 621 children with mild or moderate-severe asthma, and total IgE levels and eosinophil counts were measured for each subject. For example, more asthmatic children bearing the non5/non5 genotype had moderate-severe asthma than children with the 5/5 genotype (5.3% vs. 1.4%, p=0.008).

[0180] Rows **702**, **704**, and **706** represent fields of data reported for children with asthma. In the Kalayci reference, factors likely to be effective in determining the severity of asthma, including ALOX5 genotype, were identified by logistic regression analyses. The cohort was split into mild and moderate-severe asthma. The Kalayci reference examined the following variables: age, gender, age of onset, skin test positivity, total IgE level, peripheral blood eosinophil count, exposure to tobacco smoke, animal ownership, family history of atopic diseases, LTC<sub>4</sub> synthase genotype, and

ALOX5 genotype. Univariate analyses were followed by multivariate logistic regression. A two-sided p-value of <0.05 was considered significant.

[0181] Rows **702**, **704**, and **706** contain study data **106** from the Kalayci reference, showing allergy study data **304**. As shown in row **702**, innate allergy data **306** was identified in terms of the asthma-associated ALOX5 genotype non5/non5 (also innate determinant data **702**). Allergy test data **308** was also identified in terms of individuals with an eosinophil count of 390. Allergy predisposition information **310** is present in the form of moderate-severe asthma symptoms in individuals with the ALOX5 non5/non5 genotype and an eosinophil count of 390. Thus, the specific innate allergy determinant (innate allergy data **306**) and allergy test data **308** among individuals experiencing moderate-severe asthma is allergy predisposition information **310** that gives an indication of differential allergy severity for that group relative to other groups.

[0182] As shown in row **704**, innate allergy data **306** was identified in terms of the ALOX5 non5/non5 allele genotype (also innate determinant data **704**). Allergy test data **308** was also identified in terms of a total IgE level of 229. Allergy predisposition information **310** is present in the form of moderate-severe symptoms observed in the ALOX5 non5/non5 allele (5.3% moderate-severe vs. 1.4% of mild) and total IgE level of 229 (229 total IgE for the moderate-severe group vs. 179 total IgE for the mild group). Thus, the specific innate allergy determinant (innate allergy data **306**) and allergy test data **308** among individuals experiencing moderate-severe asthma is allergy predisposition information **310** that gives an indication of differential allergy severity for that group relative to other groups.

[0183] As shown in row **706**, innate allergy data **306** was identified in terms of the ALOX5 non5/non5 allele genotype (also innate determinant data **704**). Allergy test data **308** was also identified in terms of an eosinophil count of 390. Allergy predisposition information **310** is present in the form of a calculated and reported odds ratio of 3.647 associated with having moderate-severe asthma in ALOX5 non5/non5 individuals compared to those with ALOX5 5/5 and ALOX5 5/non5 alleles. A multivariate analysis identified family history, eosinophil count, and ALOX5 genotype as predictive of disease severity. Thus, the specific innate allergy determinant (innate allergy data **306**) and allergy test data **308** among individuals experiencing moderate-severe asthma is allergy predisposition information **310** that gives an indication of differential allergy severity for that group relative to other groups.

[0184] FIG. 8 illustrates hypothetical alternative embodiments of study data **106** associated with the research system **100** of FIG. 1, with specific examples of allergy study data **304**.

[0185] As shown in row **802** relating to peanut allergy, innate determinant data **802**, such as a particular DNA sequence, may be used to find innate allergy data **306** that associates the particular DNA sequence with, for example, peanut allergy. Further, allergy test data **308** also may be accessed, such as a measurement of specific IgE to a peanut allergen for a given individual or population. The particular DNA sequence that is associated with peanut allergy and the measurement of specific IgE to a peanut allergen may then be linked to peanut allergy symptoms by the allergy data analysis system **102** and/or allergy data association logic **126** and/or allergy predisposition information logic **128** to

identify allergy predisposition information 310. This is then an example of ingestion-dependent allergy predisposition information 810. The allergy data analysis system 102 may then present a signal related to the ingestion-dependent allergy predisposition information 810 in response to accessing the allergy test data 308 to identify, based on the at least one innate allergy determinant (innate allergy data 306), the allergy predisposition information.

[0186] As shown in row 804, also relating to peanut allergy, the innate determinant data and/or innate allergy data 306 may be an epigenetic peanut allergy determinant, e.g., a methylation pattern for a certain gene. The allergy test data 308 may be, for example, a total IgE measurement associated with exposure to a peanut allergen. Ingestion-dependent allergy predisposition information 810 may be, for example, the degree of peanut allergy symptoms associated with the epigenetic peanut allergy determinant and the total IgE measurement, as determined by the allergy data analysis system 102 and/or allergy data association logic 126 and/or allergy predisposition information logic 128. The allergy data analysis system 102 may then present a signal related to the ingestion-dependent allergy predisposition information 810 in response to accessing the allergy test data 308 to identify, based on the at least one innate allergy determinant (innate allergy data 306), the allergy predisposition information, in this case ingestion-dependent allergy predisposition information 810.

[0187] As shown in row 806, also relating to peanut allergy, the innate determinant data and/or innate allergy data 306 may be a gene expression peanut allergy determinant, e.g., a certain mRNA or protein level corresponding to a certain gene. The allergy test data 308 may be an eosinophil cell count associated with exposure to a peanut allergen. Ingestion-dependent allergy predisposition information 810 may be, for example, the incidence of peanut allergy symptoms associated with the gene expression peanut allergy determinant and the eosinophil count, as determined by the allergy data analysis system 102 and/or allergy data association logic 126 and/or allergy predisposition information logic 128. The allergy data analysis system 102 may then present a signal related to the ingestion-dependent allergy predisposition information 810 in response to accessing the allergy test data 308 to identify, based on the at least one innate allergy determinant (innate allergy data 306), the allergy predisposition information, in this case ingestion-dependent allergy predisposition information 810.

[0188] Further, for any of the examples of rows 802 through 806, the allergy data analysis system 102 and/or allergy data association logic 126 and/or allergy predisposition information logic 128 may access subpopulation identifier data 312. For example, the allergy data analysis system 102 and/or allergy data association logic 126 and/or allergy predisposition information logic 128 may access family history to associate the DNA sequence determinant with a specific portion of the family tree. This may thus identify a subpopulation associated with the innate allergy data 306, and/or the allergy test data 308 and/or the ingestion-dependent allergy predisposition information 810.

[0189] Alternatively, the allergy data analysis system 102 and/or allergy data association logic 126 and/or allergy predisposition information logic 128 may access subpopulation identifier data 312 such as demographic group information associated with the epigenetic peanut allergy determinant, so as to identify a demographic subpopulation

linked to the innate allergy data 306, and/or the allergy test data 308 and/or the ingestion-dependent allergy predisposition information 810.

[0190] Alternatively, the allergy data analysis system 102 and/or allergy data association logic 126 and/or allergy predisposition information logic 128 may access subpopulation identifier data 312 such as ethnic group information to make an association with the gene expression peanut allergy determinant, so as to identify an ethnic subpopulation linked to the innate allergy data 306, and/or the allergy test data 308 and/or the ingestion-dependent allergy predisposition information 810.

[0191] In a case where the allergy test data 308 is a test result indicating an allergic response to a specific food item, subpopulation identifier data 312 may be populations following a diet that is rich in that food item (e.g., fava beans in a Mediterranean diet). Thus subpopulation identifier data 312 may be associated with allergy test data 308, as well as innate allergy data 306.

[0192] FIG. 9 illustrates an operational flow 900 representing example operations related to computational systems for biomedical data. In FIG. 9 and in following figures that include various examples of operational flows, discussion, and explanation may be provided with respect to the above-described examples of FIGS. 1-8, and/or with respect to other examples and contexts. However, it should be understood that the operational flows may be executed in a number of other environment and contexts, and/or in modified versions of FIGS. 1-8. Also, although the various operational flows are presented in the sequence(s) illustrated, it should be understood that the various operations may be performed in other orders than those which are illustrated, or may be performed concurrently.

[0193] After a start operation, operation 910 shows accepting an input providing innate determinant data from at least one sample. The input and/or query parameter may be accepted through a user interface 132 from a researcher 104.

[0194] For example, the allergy data association logic 126 of the allergy data analysis system 102 may receive a designation of at least one innate determinant datum, such as, for example, one or more innate determinant data for which allergy test data 308 is available. More specifically, this could be an individual's genetic information, or defined innate determinant data such as, for example, a known genetic sample containing a specific STAT6 gene sequence associated with nut allergy. See Amoli et al., "Polymorphism in the STAT6 gene encodes risk for nut allergy," *Genes & Immunity*, vol. 3, pp. 220-224 (2002), the "Amoli reference," which is incorporated herein in its entirety.

[0195] Operation 920 depicts accessing a dataset to identify, based on the innate determinant data, at least one innate allergy determinant in the at least one sample. For example, the allergy data association logic 126 and/or allergy predisposition information logic 128 of the allergy data analysis system 102 may apply the input to a clinical trial database to access study data 106 associating the input innate determinant data with an innate allergy determinant, i.e., innate allergy data 306. For example, as discussed above, the Kalayci reference screened individuals for specific ALOX5 genotype data, and then associated that data with asthma. Thus, ALOX5 genotypes associated with asthma are innate allergy determinants.

[0196] Operation 930 illustrates accessing an allergy test dataset to identify, based on the at least one innate allergy



determinant, allergy predisposition information. For example, the allergy data association logic 126 and/or allergy predisposition information logic 128 of the allergy data analysis system 102 may, as discussed above in the context of the Kalayci reference, access an allergy test dataset based on identification of asthma as the innate allergy determinant. The allergy test dataset, i.e., allergy test data 308, could be, e.g., eosinophil count data associated with asthma and/or asthma severity. Based on the combined innate allergy determinant and allergy test data, the allergy data association logic 126 and/or allergy predisposition information logic 128 of the allergy data analysis system 102 may identify allergy predisposition information. In the Kalayci reference discussed above, the allergy predisposition information was, for example, an odds ratio of having moderate-severe asthma of 3.647 in ALOX5 non5/non5 individuals as opposed to individuals having other ALOX5 alleles. While this odds ratio is a measure of the event frequency of the data measured in the Kalayci reference, the methods and systems herein may apply such statistical measures to estimate predisposition to asthma in individuals and/or populations at large having samples exhibiting the specific innate allergy determinant and the allergy test data.

[0197] Operation 940 illustrates presenting a signal related to ingestion-dependent allergy predisposition information in response to accessing the allergy test dataset to identify, based on the at least one innate allergy determinant, the allergy predisposition information. For example, the allergy data association logic 126 and/or allergy predisposition information logic 128 of the allergy data analysis system 102 may present a signal related to ingestion-dependent allergy predisposition information to a researcher 104 via a user interface 132. One example would be the presentation of the specific ALOX5 genotype data and eosinophil count data associated with asthma and asthma severity, discussed in the context of the Kalayci reference, as the signal related to allergy predisposition information. Similarly, a specific peanut allergy innate determinant, specific peanut allergy test data, and associated defined peanut allergy level could be presented as the signal related to ingestion-dependent allergy predisposition information in response to accessing the peanut allergy test dataset to identify, based on the at least one peanut allergy innate determinant, allergy predisposition information for peanut allergy.

[0198] Optionally, the allergy predisposition information and/or ingestion-dependent allergy predisposition information are assigned to at least one memory. For example, the allergy predisposition information and/or ingestion-dependent allergy predisposition information may be assigned to one or more of the various (types of) databases referenced above, such as the relational and/or object-oriented database (s), or to another type of memory, not explicitly mentioned.

[0199] In this regard, it should be understood that the signal may first be encoded and/or represented in digital form (i.e., as digital data), prior to the assignment to the at least one memory. For example, a digitally-encoded representation of allergy predisposition information may be stored in a local memory, or may be transmitted for storage in a remote memory.

[0200] Thus, an operation may be performed related either to a local or remote storage of the digital data, or to another type of transmission of the digital data. Of course, as discussed herein, operations also may be performed related to accessing, querying, processing, recalling, or otherwise

obtaining the digital data from a memory, including, for example, receiving a transmission of the digital data from a remote memory. Accordingly, such operation(s) may involve elements including at least an operator (e.g., either human or computer) directing the operation, a transmitting computer, and/or a receiving computer, and should be understood to occur within the United States as long as at least one of these elements resides in the United States.

[0201] FIG. 10 illustrates alternative embodiments of the example operational flow 900 of FIG. 9. FIG. 10 illustrates example embodiments where the accepting operation 910 may include at least one additional operation. Additional operations may include operation 1002 and/or operation 1004.

[0202] Operation 1002 depicts accepting an input providing genomic data, epigenetic data, or gene expression data from at least one sample. For example, the allergy data analysis system 102 and/or the allergy data association logic 126 and/or allergy predisposition information logic 128 may accept an electronic transmission from a remote user interface 132 that provides, for example, an individual's genetic sequence data.

[0203] Operation 1004 depicts accepting an input providing ethnic, racial, or demographic data as the innate determinant data from at least one sample. For example, the allergy data analysis system 102 and/or the allergy data association logic 126 and/or allergy predisposition information logic 128 may accept via a user interface 132, for example, ethnic origin data for a population as the innate determinant data from at least one sample.

[0204] FIG. 11 illustrates alternative embodiments of the example operational flow 900 of FIG. 9. FIG. 11 illustrates example embodiments where the accessing operation 920 may include at least one additional operation. Additional operations may include operation 1102, 1104, and/or operation 1106.

[0205] Operation 1102 depicts accessing a clinical trial dataset, or an informal allergy study dataset to identify, based on the innate determinant data, at least one innate allergy determinant in the at least one sample. For example, the allergy data analysis system 102 and/or the allergy data association logic 126 and/or allergy predisposition information logic 128 may access, for example, at least data from the cross-sectional ALEX clinical trial reported in the Eder reference, discussed above, which identified CARD4/NOD1 genotypes as innate determinants associated with asthma.

[0206] Operation 1104 depicts accessing a dataset to identify, based on the innate determinant data, at least one gene sequence allergy determinant, single nucleotide polymorphism allergy determinant, or haplotype allergy determinant in the at least one sample. For example, the allergy data analysis system 102 and/or the allergy data association logic 126 and/or allergy predisposition information logic 128 may access, for example, a STAT6 DNA sequence associated with nut allergy as the at least one innate allergy determinant in the at least one sample.

[0207] Operation 1106 depicts accessing a dataset to identify, based on the innate determinant data, at least one human leukocyte antigen sequence allergy determinant in the at least one sample. For example, the allergy data analysis system 102 and/or the allergy data association logic 126 and/or allergy predisposition information logic 128 may



access an HLA DR9 sequence associated with penicillin allergy as the at least one innate allergy determinant in the at least one sample.

[0208] FIG. 12 illustrates alternative embodiments of the example operational flow 900 of FIG. 9. FIG. 12 illustrates example embodiments where the accessing operation 920 may include at least one additional operation. Additional operations may include operation 1202, and/or operation 1204.

[0209] Operation 1202 depicts accessing a dataset to identify, based on the innate determinant data, at least one atopic allergy determinant in the at least one sample. For example, the allergy data analysis system 102 and/or the allergy data association logic 126 and/or allergy predisposition information logic 128 may access an epigenetic sequence associated with atopic dermatitis as the at least one innate allergy determinant in the at least one sample.

[0210] Operation 1204 depicts accessing a dataset to identify, based on the innate determinant data, at least one T cell allergy determinant in the at least one sample. For example, the allergy data analysis system 102 and/or the allergy data association logic 126 and/or allergy predisposition information logic 128 may access, for example, a Th2 helper cell population determinant as the at least one innate allergy determinant in the at least one sample.

[0211] FIG. 13 illustrates alternative embodiments of the example operational flow 900 of FIG. 9. FIG. 13 illustrates example embodiments where the accessing operation 930 may include at least one additional operation. Additional operations may include operation 1302, 1304, 1306, and/or operation 1308.

[0212] Operation 1302 depicts accessing a total IgE dataset or a specific IgE dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information. For example, the allergy data analysis system 102 and/or the allergy data association logic 126 and/or allergy predisposition information logic 128 may access, for example, data containing at least specific penicillin IgE level data associated with penicillin allergy as reported in the Yang reference, discussed above.

[0213] Operation 1304 depicts accessing a quantitative, allergen-specific, human serum IgE dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information. For example, the allergy data analysis system 102 and/or the allergy data association logic 126 and/or allergy predisposition information logic 128 may access, for example, data from a commercially available quantitative serum IgE test, such as Pharmacia's CAP test (as used in the Eder reference) and CAP fluorezymeimmunoassay (FEIA).

[0214] Operation 1306 depicts accessing a radioallergosorbent test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information. For example, the allergy data analysis system 102 and/or the allergy data association logic 126 and/or allergy predisposition information logic 128 may access, for example, data from a commercially available radioallergosorbent (RAST) test, such as, for example, FDA-approved RAST tests.

[0215] FIG. 14 illustrates alternative embodiments of the example operational flow 900 of FIG. 9. FIG. 14 illustrates example embodiments where the accessing operation 930

may include at least one additional operation. Additional operations may include operation 1402, 1404, 1406, and/or operation 1408.

[0216] Operation 1402 depicts accessing a skin test dataset or a patch test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information. For example, the allergy data analysis system 102 and/or the allergy data association logic 126 and/or allergy predisposition information logic 128 may access, for example, peanut allergy skin test results for an individual bearing a specific STAT6 genotype associated with nut allergy.

[0217] Operation 1404 depicts accessing a skin prick, skin scratch, or intradermal skin test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information. For example, the allergy data analysis system 102 and/or the allergy data association logic 126 and/or allergy predisposition information logic 128 may access, for example, peanut allergy skin prick test results for an individual bearing a specific STAT6 genotype associated with nut allergy.

[0218] Operation 1406 depicts accessing a diet elimination dataset or a food challenge test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information. For example, the allergy data analysis system 102 and/or the allergy data association logic 126 and/or allergy predisposition information logic 128 may access, for example, peanut food challenge test results for an individual bearing a specific STAT6 genotype associated with nut allergy.

[0219] Operation 1408 depicts accessing an eosinophil count dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information. For example, the allergy data analysis system 102 and/or the allergy data association logic 126 and/or allergy predisposition information logic 128 may access, for example, blood serum eosinophil numbers for an individual bearing a specific STAT6 genotype associated with nut allergy.

[0220] FIG. 15 illustrates alternative embodiments of the example operational flow 900 of FIG. 9. FIG. 15 illustrates example embodiments where the accessing operation 930 may include at least one additional operation. Additional operations may include operation 1502, and/or operation 1504.

[0221] Operation 1502 depicts accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, statistically-characterized allergy predisposition information. For example, the allergy data analysis system 102 and/or the allergy data association logic 126 and/or allergy predisposition information logic 128 may identify, based on an ALOX5 non5/non5 innate allergy determinant, for example, blood serum eosinophil numbers of 390 that are statistically higher in individuals with moderate-severe symptoms than in individuals with mild asthma symptoms (p-value=0.002; See Kalayci reference and FIG. 7).

[0222] Operation 1504 depicts accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, statistically-characterized allergy predisposition information indicating the absence of an allergy predisposition. For example, the allergy data analysis system 102 and/or the allergy data association logic 126 and/or allergy predisposition information logic 128 may identify, based on an HLA DR14.1 genotype innate penicillin allergy

determinant, for example, individuals with positive IgE for penicillin with a statistically significant absence of an immediate response and/or urticaria symptoms (p-value <0.05 vs. control; See Yang reference and FIG. 6).

[0223] FIG. 16 illustrates alternative embodiments of the example operational flow 900 of FIG. 9. FIG. 16 illustrates example embodiments where the presenting operation 940 may include at least one additional operation. Additional operations may include operation 1602.

[0224] Operation 1602 depicts presenting a signal related to ingestion-dependent allergy predisposition information to a user at a user interface in response to accessing the allergy test dataset to identify, based on the at least one innate allergy determinant, the allergy predisposition information. For example, the allergy data analysis system 102 and/or the allergy data association logic 126 and/or allergy predisposition information logic 128 may present, for example, a signal related to ingestion-dependent allergy predisposition information associated with an 80% incidence of at least one allergy among individuals sharing a particular innate allergy determinant and particular allergy test data, to a user at a user interface.

[0225] FIG. 17 illustrates an operational flow 1700 representing example operations related to computational systems for biomedical data. In FIG. 17, discussion, and explanation may be provided with respect to the above-described examples of FIGS. 1-8, and/or with respect to other examples and contexts. However, it should be understood that the operational flow may be executed in a number of other environment and contexts, and/or in modified versions of FIGS. 1-8. Also, although the operational flow is presented in the sequence illustrated, it should be understood that the various operations may be performed in other orders than those which are illustrated, or may be performed concurrently.

[0226] After a start operation, operation 1710 shows accepting an input identifying at least one allergic reaction to an allergen. The input may be accepted through a user interface 132 from a researcher 104.

[0227] For example, the allergy data association logic 126 of the allergy data analysis system 102 may receive a designation of at least one allergic reaction to an allergen, such as, for example, one or more allergens for which allergy test data 308 is available. More specifically, this could be a known allergen such as, for example, peanuts, or a drug such as aspirin.

[0228] Operation 1720 depicts accessing a dataset to identify at least one innate allergy determinant of the at least one allergic reaction in a population. For example, the allergy data association logic 126 and/or allergy predisposition information logic 128 of the allergy data analysis system 102 may access a published study associating an allergy with a specific genetic sequence, or innate allergy determinant, i.e., innate allergy data 306. For example, data could be accessed to identify genotype data associated with peanut allergy, such as a particular STAT6 genotype. See the Amoli reference, discussed above.

[0229] Operation 1740 depicts accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, a portion of the population with a predisposition to the allergic reaction. For example, the allergy data association logic 126 and/or allergy predisposition information logic 128 of the allergy data analysis system 102 may access an allergy test dataset (e.g., specific IgE test, skin test,

food challenge test, etc.), based on the innate allergy determinant. For example, data could be accessed to identify the portion of the population having a specific STAT6 genotype associated with nut allergy, skin test data associated with peanut allergy, and a certain level of peanut allergy symptoms, as the allergy predisposition information.

[0230] Operation 1760 depicts calculating, based on the portion of the population with a predisposition to the allergic reaction, an allergic index for the population. For example, the allergy data association logic 126 and/or allergy predisposition information logic 128 of the allergy data analysis system 102 may calculate, based on the allergy predisposition information for a portion of the population, an allergic index that signifies the likelihood of allergic reaction in individuals in the portion of the population. Such a calculation may be as simple as a percentage of individuals with a predisposition relative to the population as a whole, or the calculation may be statistically more sophisticated, taking into account confidence intervals or other measures of probability of experiencing the allergic reaction.

[0231] Operation 1780 depicts presenting a signal related to the allergic index for the population in response to calculating, based on the portion of the population with a predisposition to the allergic reaction, the allergic index for the population. For example, the allergy data association logic 126 and/or allergy predisposition information logic 128 of the allergy data analysis system 102 may present a signal related to a 70% allergic index for peanut allergy in people of Icelandic descent with a certain specific IgE level to peanuts.

[0232] FIG. 18 illustrates an operational flow 1800 representing example operations related to computational systems for biomedical data. In FIG. 18, discussion, and explanation may be provided with respect to the above-described examples of FIGS. 1-8, and/or with respect to other examples and contexts. However, it should be understood that the operational flow may be executed in a number of other environment and contexts, and/or in modified versions of FIGS. 1-8. Also, although the operational flow is presented in the sequence illustrated, it should be understood that the various operations may be performed concurrently.

[0233] After a start operation, operation 1810 shows accepting an input providing innate determinant data from at least one sample at one or more user interfaces. For example, the input may be accepted through a user interface 132 from a researcher 104.

[0234] For example, the allergy data association logic 126 of the allergy data analysis system 102 may receive a designation of innate determinant data at one or more user interfaces. More specifically, the innate determinant data could be a genetic sequence, an epigenetic determinant, or a gene expression determinant.

[0235] Operation 1820 depicts transmitting data from the one or more user interfaces to at least one data analysis system, the data including at least the innate determinant data, the data analysis system being capable of accessing a dataset to identify, based on the innate determinant data, at least one innate allergy determinant in the at least one sample; accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information; presenting a signal related to ingestion-dependent allergy predisposition information in response to accessing the allergy test dataset to identify, based on the at least one innate allergy determinant, the

allergy predisposition information; and the data analysis system further being capable of sending a signal to either the one or more user interfaces or a different user interface in response to the allergy predisposition information, which signal transmits the ingestion-dependent allergy predisposition information.

[0236] For example, an input from a user interface 132 from a researcher 104 may be sent to the allergy data analysis system 102, the input including, for example, an individual's genetic sequence. The data analysis system 102 and/or allergy data association logic 126 and/or allergy predisposition information logic 128 is capable of accessing a dataset to identify, based on the individual's genetic data, at least one innate allergy determinant in the at least one sample, for example, a genetic sequence associated with chocolate allergy. The data analysis system 102 and/or allergy data association logic 126 and/or allergy predisposition information logic 128 is further capable of accessing an allergy test dataset such as a life history of exposure to chocolate to identify, based on the genetic sequence associated with chocolate allergy, allergy predisposition information, such as the genetic sequence associated with chocolate allergy, a high consumption of chocolate over time, and an associated level of chocolate allergy symptoms. The data analysis system 102 and/or allergy data association logic 126 and/or allergy predisposition information logic 128 is also capable of presenting a signal related to chocolate allergy predisposition information, including the genetic sequence associated with chocolate allergy and life history of exposure to chocolate, the chocolate allergy predisposition information associated with a significantly elevated risk of, for example, anaphylaxis upon exposure to chocolate. The data analysis system 102 and/or allergy data association logic 126 and/or allergy predisposition information logic 128 is further capable of sending the chocolate allergy predisposition information to, for example the researcher 104 at the user interface 132.

[0237] FIG. 19 illustrates a partial view of an example computer program product 1900 that includes a computer program 1904 for executing a computer process on a computing device. An embodiment of the example computer program product 1900 is provided using a signal bearing medium 1902, and may include one or more instructions for accepting an input providing innate determinant data from at least one sample; one or more instructions for accessing a dataset to identify, based on the innate determinant data, at least one innate allergy determinant in the at least one sample; one or more instructions for accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information; and presenting a signal related to ingestion-dependent allergy predisposition information in response to accessing the allergy test dataset to identify, based on the at least one innate allergy determinant, the allergy predisposition information. The one or more instructions may be, for example, computer executable and/or logic-implemented instructions. In one implementation, the signal-bearing medium 1902 may include a computer-readable medium 1906. In one implementation, the signal bearing medium 1902 may include a recordable medium 1908. In one implementation, the signal bearing medium 1902 may include a communications medium 1910.

[0238] FIG. 20 illustrates an example system 2000 in which embodiments may be implemented. The system 2000

includes a computing system environment. The system 2000 also illustrates the researcher 104 using a research device 2004, which is optionally shown as being in communication with a computing device 2002 by way of an optional coupling 2006. The optional coupling 2006 may represent a local, wide-area, or peer-to-peer network, or may represent a bus that is internal to a computing device (e.g., in example embodiments in which the computing device 2002 is contained in whole or in part within the research device 2004). A storage medium 2008 may be any computer storage media.

[0239] The computing device 2002 includes computer-executable instructions 2010 that when executed on the computing device 2002 cause the computing device 2002 to accept an input providing innate determinant data from at least one sample; access a dataset to identify, based on the innate determinant data, at least one innate allergy determinant in the at least one sample; access an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information; and present a signal related to the ingestion-dependent allergy predisposition information in response to accessing the allergy test dataset to identify, based on the at least one innate allergy determinant, the allergy predisposition information. As referenced above and as shown in FIG. 20, in some examples, the computing device 2002 may optionally be contained in whole or in part within the research device 2004.

[0240] In FIG. 20, then, the system 2000 includes at least one computing device (e.g., 2002 and/or 2004). The computer-executable instructions 2010 may be executed on one or more of the at least one computing device. For example, the computing device 2002 may implement the computer-executable instructions 2010 and output a result to (and/or receive data from) the computing (research) device 2004. Since the computing device 2002 may be wholly or partially contained within the computing (research) device 2004, the research device 2004 also may be said to execute some or all of the computer-executable instructions 2010, in order to be caused to perform or implement, for example, various ones of the techniques described herein, or other techniques.

[0241] The research device 2004 may include, for example, a portable computing device, workstation, or desktop computing device. In another example embodiment, the computing device 2002 is operable to communicate with the device 2004 associated with the researcher 104 to receive information about the input from the researcher 104 for performing data access and data associations and presenting a signal(s) relating to allergy predisposition information.

[0242] Although a user or researcher 104 is shown/described herein as a single illustrated figure, those skilled in the art will appreciate that a user or researcher 104 may be representative of a human user, a robotic user (e.g., computational entity), and/or substantially any combination thereof (e.g., a user may be assisted by one or more robotic agents). In addition, a user or researcher 104, as set forth herein, although shown as a single entity may in fact be composed of two or more entities. Those skilled in the art will appreciate that, in general, the same may be said of "sender" and/or other entity-oriented terms as such terms are used herein.

[0243] One skilled in the art will recognize that the herein described components (e.g., steps), devices, and objects and the discussion accompanying them are used as examples for the sake of conceptual clarity and that various configuration

modifications are within the skill of those in the art. Consequently, as used herein, the specific exemplars set forth and the accompanying discussion are intended to be representative of their more general classes. In general, use of any specific exemplar herein is also intended to be representative of its class, and the non-inclusion of such specific components (e.g., steps), devices, and objects herein should not be taken as indicating that limitation is desired.

**[0244]** Those skilled in the art will appreciate that the foregoing specific exemplary processes and/or devices and/or technologies are representative of more general processes and/or devices and/or technologies taught elsewhere herein, such as in the claims filed herewith and/or elsewhere in the present application.

**[0245]** Those having skill in the art will recognize that the state of the art has progressed to the point where there is little distinction left between hardware and software implementations of aspects of systems; the use of hardware or software is generally (but not always, in that in certain contexts the choice between hardware and software can become significant) a design choice representing cost vs. efficiency tradeoffs. Those having skill in the art will appreciate that there are various vehicles by which processes and/or systems and/or other technologies described herein can be effected (e.g., hardware, software, and/or firmware), and that the preferred vehicle will vary with the context in which the processes and/or systems and/or other technologies are deployed. For example, if an implementer determines that speed and accuracy are paramount, the implementer may opt for a mainly hardware and/or firmware vehicle; alternatively, if flexibility is paramount, the implementer may opt for a mainly software implementation; or, yet again alternatively, the implementer may opt for some combination of hardware, software, and/or firmware. Hence, there are several possible vehicles by which the processes and/or devices and/or other technologies described herein may be effected, none of which is inherently superior to the other in that any vehicle to be utilized is a choice dependent upon the context in which the vehicle will be deployed and the specific concerns (e.g., speed, flexibility, or predictability) of the implementer, any of which may vary. Those skilled in the art will recognize that optical aspects of implementations will typically employ optically-oriented hardware, software, and/or firmware.

**[0246]** The foregoing detailed description has set forth various embodiments of the devices and/or processes via the use of block diagrams, flowcharts, and/or examples. Insofar as such block diagrams, flowcharts, and/or examples contain one or more functions and/or operations, it will be understood by those within the art that each function and/or operation within such block diagrams, flowcharts, or examples can be implemented, individually and/or collectively, by a wide range of hardware, software, firmware, or virtually any combination thereof. In one embodiment, several portions of the subject matter described herein may be implemented via Application Specific Integrated Circuits (ASICs), Field Programmable Gate Arrays (FPGAs), digital signal processors (DSPs), or other integrated formats. However, those skilled in the art will recognize that some aspects of the embodiments disclosed herein, in whole or in part, can be equivalently implemented in integrated circuits, as one or more computer programs running on one or more computers (e.g., as one or more programs running on one or more computer systems), as one or more programs running on one

or more processors (e.g., as one or more programs running on one or more microprocessors), as firmware, or as virtually any combination thereof, and that designing the circuitry and/or writing the code for the software and/or firmware would be well within the skill of one of skill in the art in light of this disclosure. In addition, those skilled in the art will appreciate that the mechanisms of the subject matter described herein are capable of being distributed as a program product in a variety of forms, and that an illustrative embodiment of the subject matter described herein applies regardless of the particular type of signal bearing medium used to actually carry out the distribution. Examples of a signal bearing medium include, but are not limited to, the following: a recordable type medium such as a floppy disk, a hard disk drive, a Compact Disc (CD), a Digital Video Disk (DVD), a digital tape, a computer memory, etc.; and a transmission type medium such as a digital and/or an analog communication medium (e.g., a fiber optic cable, a waveguide, a wired communications link, a wireless communication link, etc.).

**[0247]** In a general sense, those skilled in the art will recognize that the various aspects described herein which can be implemented, individually and/or collectively, by a wide range of hardware, software, firmware, or any combination thereof can be viewed as being composed of various types of “electrical circuitry.” Consequently, as used herein “electrical circuitry” includes, but is not limited to, electrical circuitry having at least one discrete electrical circuit, electrical circuitry having at least one integrated circuit, electrical circuitry having at least one application specific integrated circuit, electrical circuitry forming a general purpose computing device configured by a computer program (e.g., a general purpose computer configured by a computer program which at least partially carries out processes and/or devices described herein, or a microprocessor configured by a computer program which at least partially carries out processes and/or devices described herein), electrical circuitry forming a memory device (e.g., forms of random access memory), and/or electrical circuitry forming a communications device (e.g., a modem, communications switch, or optical-electrical equipment). Those having skill in the art will recognize that the subject matter described herein may be implemented in an analog or digital fashion or some combination thereof.

**[0248]** Those skilled in the art will recognize that it is common within the art to describe devices and/or processes in the fashion set forth herein, and thereafter use engineering practices to integrate such described devices and/or processes into data processing systems. That is, at least a portion of the devices and/or processes described herein can be integrated into a data processing system via a reasonable amount of experimentation. Those having skill in the art will recognize that a typical data processing system generally includes one or more of a system unit housing, a video display device, a memory such as volatile and non-volatile memory, processors such as microprocessors and digital signal processors, computational entities such as operating systems, drivers, graphical user interfaces, and applications programs, one or more interaction devices, such as a touch pad or screen, and/or control systems including feedback loops and control motors (e.g., feedback for sensing position and/or velocity; control motors for moving and/or adjusting components and/or quantities). A typical data processing system may be implemented utilizing any suitable commer-

cially available components, such as those typically found in data computing/communication and/or network computing/communication systems.

**[0249]** All of the above U.S. patents, U.S. patent application publications, U.S. patent applications, foreign patents, foreign patent applications and non-patent publications referred to in this specification and/or listed in any Application Data Sheet are incorporated herein by reference, in their entireties.

**[0250]** The herein described subject matter sometimes illustrates different components contained within, or connected with, different other components. It is to be understood that such depicted architectures are merely exemplary, and that in fact many other architectures can be implemented which achieve the same functionality. In a conceptual sense, any arrangement of components to achieve the same functionality is effectively “associated” such that the desired functionality is achieved. Hence, any two components herein combined to achieve a particular functionality can be seen as “associated with” each other such that the desired functionality is achieved, irrespective of architectures or intermedial components. Likewise, any two components so associated can also be viewed as being “operably connected”, or “operably coupled,” to each other to achieve the desired functionality, and any two components capable of being so associated can also be viewed as being “operably couplable,” to each other to achieve the desired functionality. Specific examples of operably couplable include but are not limited to physically mateable and/or physically interacting components and/or wirelessly interactable and/or wirelessly interacting components and/or logically interacting and/or logically interactable components.

**[0251]** While certain features of the described implementations have been illustrated as disclosed herein, many modifications, substitutions, changes and equivalents will now occur to those skilled in the art. It is, therefore, to be understood that the appended claims are intended to cover all such modifications and changes as fall within the true spirit of the embodiments of the invention.

**[0252]** With respect to the use of substantially any plural and/or singular terms herein, those having skill in the art can translate from the plural to the singular and/or from the singular to the plural as is appropriate to the context and/or application. The various singular/plural permutations are not expressly set forth herein for sake of clarity.

**[0253]** While particular aspects of the present subject matter described herein have been shown and described, it will be apparent to those skilled in the art that, based upon the teachings herein, changes and modifications may be made without departing from the subject matter described herein and its broader aspects and, therefore, the appended claims are to encompass within their scope all such changes and modifications as are within the true spirit and scope of the subject matter described herein. Furthermore, it is to be understood that the invention is defined by the appended claims. It will be understood by those within the art that, in general, terms used herein, and especially in the appended claims (e.g., bodies of the appended claims) are generally intended as “open” terms (e.g., the term “including” should be interpreted as “including but not limited to,” the term “having” should be interpreted as “having at least,” the term “includes” should be interpreted as “includes but is not limited to,” etc.). It will be further understood by those within the art that if a specific number of an introduced claim

recitation is intended, such an intent will be explicitly recited in the claim, and in the absence of such recitation no such intent is present. For example, as an aid to understanding, the following appended claims may contain usage of the introductory phrases “at least one” and “one or more” to introduce claim recitations. However, the use of such phrases should not be construed to imply that the introduction of a claim recitation by the indefinite articles “a” or “an” limits any particular claim containing such introduced claim recitation to inventions containing only one such recitation, even when the same claim includes the introductory phrases “one or more” or “at least one” and indefinite articles such as “a” or “an” (e.g., “a” and/or “an” should typically be interpreted to mean “at least one” or “one or more”); the same holds true for the use of definite articles used to introduce claim recitations. In addition, even if a specific number of an introduced claim recitation is explicitly recited, those skilled in the art will recognize that such recitation should typically be interpreted to mean at least the recited number (e.g., the bare recitation of “two recitations,” without other modifiers, typically means at least two recitations, or two or more recitations). Furthermore, in those instances where a convention analogous to “at least one of A, B, and C, etc.” is used, in general such a construction is intended in the sense one having skill in the art would understand the convention (e.g., “a system having at least one of A, B, and C” would include but not be limited to systems that have A alone, B alone, C alone, A and B together, A and C together, B and C together, and/or A, B, and C together, etc.). In those instances where a convention analogous to “at least one of A, B, or C, etc.” is used, in general such a construction is intended in the sense one having skill in the art would understand the convention (e.g., “a system having at least one of A, B, or C” would include but not be limited to systems that have A alone, B alone, C alone, A and B together, A and C together, B and C together, and/or A, B, and C together, etc.). It will be further understood by those within the art that virtually any disjunctive word and/or phrase presenting two or more alternative terms, whether in the description, claims, or drawings, should be understood to contemplate the possibilities of including one of the terms, either of the terms, or both terms. For example, the phrase “A or B” will be understood to include the possibilities of “A” or “B” or “A and B.”

**[0254]** With respect to the appended claims, those skilled in the art will appreciate that recited operations therein may generally be performed in any order. Examples of such alternate orderings may include overlapping, interleaved, interrupted, reordered, incremental, preparatory, supplemental, simultaneous, reverse, or other variant orderings, unless context dictates otherwise. With respect to context, even terms like “responsive to,” “related to,” or other past-tense adjectives are generally not intended to exclude such variants, unless context dictates otherwise.

1. A method for determining allergy predisposition comprising:

- accepting an input providing innate determinant data from at least one sample;
- accessing a dataset to identify, based on the innate determinant data, at least one innate allergy determinant in the at least one sample;
- accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information; and

presenting a signal related to ingestion-dependent allergy predisposition information in response to accessing the allergy test dataset to identify, based on the at least one innate allergy determinant, the allergy predisposition information.

2. The method of claim 1 wherein accepting an input providing innate determinant data from at least one sample comprises:

- accepting an input providing genetic data, epigenetic data, or gene expression data from at least one sample.

3. The method of claim 1 wherein accepting an input providing innate determinant data from at least one sample comprises:

- accepting an input providing ethnic, racial, or demographic data as the innate determinant data from at least one sample.

4. The method of claim 1 wherein accessing a dataset to identify, based on the innate determinant data, at least one innate allergy determinant in the at least one sample comprises:

- accessing a clinical trial dataset, or an informal allergy study dataset to identify, based on the innate determinant data, at least one innate allergy determinant in the at least one sample.

5. The method of claim 1 wherein accessing a dataset to identify, based on the innate determinant data, at least one innate allergy determinant in the at least one sample comprises:

- accessing a dataset to identify, based on the innate determinant data, at least one gene sequence allergy determinant, single nucleotide polymorphism allergy determinant, or haplotype allergy determinant in the at least one sample.

6. The method of claim 1 wherein accessing a dataset to identify, based on the innate determinant data, at least one innate allergy determinant in the at least one sample comprises:

- accessing a dataset to identify, based on the innate determinant data, at least one human leukocyte antigen sequence allergy determinant in the at least one sample.

7. The method of claim 1 wherein accessing a dataset to identify, based on the innate determinant data, at least one innate allergy determinant in the at least one sample comprises:

- accessing a dataset to identify, based on the innate determinant data, at least one atopic allergy determinant in the at least one sample.

8. The method of claim 1 wherein accessing a dataset to identify, based on the innate determinant data, at least one innate allergy determinant in the at least one sample comprises:

- accessing a dataset to identify, based on the innate determinant data, at least one T cell allergy determinant in the at least one sample.

9. The method of claim 1 wherein accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information comprises:

- accessing a total IgE dataset or a specific IgE dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information.

10. The method of claim 1 wherein accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information comprises:

- accessing a quantitative, allergen-specific, human serum IgE dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information.

11. The method of claim 1 wherein accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information comprises:

- accessing a radioallergosorbent test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information.

12. The method of claim 1 wherein accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information comprises:

- accessing a serum immunoglobulin electrophoresis test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information.

13. The method of claim 1 wherein accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information comprises:

- accessing a skin test dataset or a patch test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information.

14. The method of claim 1 wherein accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information comprises:

- accessing a skin prick, skin scratch, or intradermal skin test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information.

15. The method of claim 1 wherein accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information comprises:

- accessing a diet elimination dataset or a food challenge test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information.

16. The method of claim 1 wherein accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information comprises:

- accessing an eosinophil count dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information.

17. The method of claim 1 wherein accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information comprises:

- accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, statistically-characterized allergy predisposition information.

18. The method of claim 1 wherein accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information comprises:

- accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, statistically-characterized allergy predisposition information indicating the absence of an allergy predisposition.

19. The method of claim 1 wherein presenting a signal related to ingestion-dependent allergy predisposition information in response to accessing the allergy test dataset to

identify, based on the at least one innate allergy determinant, the allergy predisposition information comprises:

presenting a signal related to ingestion-dependent allergy predisposition information to a user at a user interface in response to accessing the allergy test dataset to identify, based on the at least one innate allergy determinant, the allergy predisposition information.

**20-21.** (canceled)

**22.** A system for determining allergy predisposition comprising:

circuitry for accepting an input providing innate determinant data from at least one sample;

circuitry for accessing a dataset to identify, based on the innate determinant data, at least one innate allergy determinant in the at least one sample;

circuitry for accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information; and

circuitry for presenting a signal related to ingestion-dependent allergy predisposition information in response to the allergy predisposition information.

**23.** The system of claim **22** wherein the circuitry for accepting an input providing innate determinant data from at least one sample comprises:

circuitry for accepting an input providing genetic data, epigenetic data, or gene expression data from at least one sample.

**24.** The system of claim **22** wherein the circuitry for accepting an input providing innate determinant data from at least one sample comprises:

circuitry for accepting an input providing ethnic, racial, or demographic data as the innate determinant data from at least one sample.

**25.** The system of claim **22** wherein the circuitry for accessing a dataset to identify, based on the innate determinant data, at least one innate allergy determinant in the at least one sample comprises:

circuitry for accessing a clinical trial dataset or an informal allergy study dataset to identify, based on the innate determinant data, at least one innate allergy determinant in the at least one sample.

**26.** The system of claim **22** wherein the circuitry for accessing a dataset to identify, based on the innate determinant data, at least one innate allergy determinant in the at least one sample comprises:

circuitry for accessing a dataset to identify, based on the innate determinant data, at least one gene sequence allergy determinant, single nucleotide polymorphism allergy determinant, or haplotype allergy determinant in the at least one sample.

**27.** The system of claim **22** wherein the circuitry for accessing a dataset to identify, based on the innate determinant data, at least one innate allergy determinant in the at least one sample comprises:

circuitry for accessing a dataset to identify, based on the innate determinant data, at least one human leukocyte antigen sequence allergy determinant in the at least one sample.

**28.** The system of claim **22** wherein the circuitry for accessing a dataset to identify, based on the innate determinant data, at least one innate allergy determinant in the at least one sample comprises:

circuitry for accessing a dataset to identify, based on the innate determinant data, at least one atopic allergy determinant in the at least one sample.

**29.** The system of claim **22** wherein the circuitry for accessing a dataset to identify, based on the innate determinant data, at least one innate allergy determinant in the at least one sample comprises:

circuitry for accessing a dataset to identify, based on the innate determinant data, at least one T cell allergy determinant in the at least one sample.

**30.** The system of claim **22** wherein the circuitry for accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information comprises:

circuitry for accessing a total IgE dataset or a specific IgE dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information.

**31.** The system of claim **22** wherein the circuitry for accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information comprises:

circuitry for accessing a quantitative, allergen-specific, human serum IgE dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information.

**32.** The system of claim **22** wherein the circuitry for accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information comprises:

circuitry for accessing a radioallergosorbent test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information.

**33.** The system of claim **22** wherein the circuitry for accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information comprises:

circuitry for accessing a serum immunoglobulin electrophoresis test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information.

**34.** The system of claim **22** wherein the circuitry for accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information comprises:

circuitry for accessing a skin test dataset or a patch test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information.

**35.** The system of claim **22** wherein the circuitry for accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information comprises:

circuitry for accessing a skin prick, skin scratch, or intradermal skin test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information.

**36.** The system of claim **22** wherein the circuitry for accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information comprises:

circuitry for accessing a diet elimination dataset or a food challenge test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information.

37. The system of claim 22 wherein the circuitry for accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information comprises:

circuitry for accessing an eosinophil count dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information.

38. The system of claim 22 wherein the circuitry for accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information comprises:

circuitry for accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, statistically-characterized allergy predisposition information.

39. The system of claim 22 wherein the circuitry for accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information comprises:

circuitry for accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, statistically-characterized allergy predisposition information indicating the absence of an allergy predisposition.

40. The system of claim 22 wherein the circuitry for presenting a signal related to ingestion-dependent allergy predisposition information in response to the allergy predisposition information comprises:

circuitry for presenting a signal related to ingestion-dependent allergy predisposition information to a user at a user interface in response to accessing the allergy test dataset to identify, based on the at least one innate allergy determinant, the allergy predisposition information.

41. (canceled)

42. A computer program product comprising:

a signal-bearing medium bearing

- (a) one or more instructions for accepting an input providing innate determinant data from at least one sample;
- (b) one or more instructions for accessing a dataset to identify, based on the innate determinant data, at least one innate allergy determinant in the at least one sample;
- (c) one or more instructions for accessing an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information; and

- (d) one or more instructions for presenting a signal related to ingestion-dependent allergy predisposition information in response to accessing the allergy test dataset to identify, based on the at least one innate allergy determinant, the allergy predisposition information.

43. The computer program product of claim 42, wherein the signal-bearing medium includes a computer-readable medium.

44. computer program product of claim 42, wherein the signal-bearing medium includes a recordable medium.

45. The computer program product of claim 42, wherein the signal-bearing medium includes a communications medium.

46. A system comprising:

a computing device; and

instructions that when executed on the computing device cause the computing device to

- (a) accept an input providing innate determinant data from at least one sample;
- (b) access a dataset to identify, based on the innate determinant data, at least one innate allergy determinant in the at least one sample;
- (c) access an allergy test dataset to identify, based on the at least one innate allergy determinant, allergy predisposition information; and
- (d) present a signal related to the ingestion-dependent allergy predisposition information in response to accessing the allergy test dataset to identify, based on the at least one innate allergy determinant, the allergy predisposition information.

47. The system of claim 46 wherein the computing device comprises:

one or more of a personal digital assistant (PDA), a laptop computer, a tablet personal computer, a networked computer, a computing system comprised of a cluster of processors, a computing system comprised of a cluster of servers, a workstation computer, and/or a desktop computer.

48. The system of claim 46 wherein the computing device is operable to receive information regarding the ingestion-dependent allergy predisposition information and to present the ingestion-dependent allergy predisposition information from at least one memory.

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